

Chettinad Health City

MEDICAL JOURNAL

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In this issue

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Personalized Medicine

Minimally Invasive Aortic Valve Replacement Does not Reduce the Incidence of Postoperative Atrial Fibrillation

Risk Factors for Coronary Artery Disease in a Semi-urban area of Tamil Nadu

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Department of Pediatrics

CHETTINAD PEDICON-2015

"COMMON PROBLEMS IN PEDIATRIC PRACTICE" - 28.02.2015



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Editorial

The Chettinad Health City Medical Journal has taken rapid strides towards establishing itself as one of the top medical journals in the country. The journal is committed to achieving high standards in terms of scientific content, and pubmed indexing in the near future. The increasing proportion of original articles will help in achieving this target.

The article on how to write a paper is a must read for all aspiring researchers and medical writers. The original article on MICS AVR is a high quality study on incidence of atrial fibrillation in patients undergoing the procedure, this is an example of a well written clinical research paper. It has a clear research question that was systematically studied and presented with great clarity; young researchers would do well to model their research papers in a similar manner.

A clear cardiology focus is apparent in this issue, with interesting perspective articles on history of CABG and personalized medicine, a timely reminder on the importance of evidence based practice of medicine. A good variety of articles, including interesting case reports that deal with topics ranging from disease epidemiology to complex operative techniques make this issue extremely diverse. The two classroom articles are concise and informative to medical students and postgraduates. This issue rounds off with an article on history of semen analysis.

Publishing research data is important for career progress, national and international recognition for the authors, hospital and universities. The art of medical scientific writing is also a valuable learning tool that creates skills like data collection, analysis and concise comprehensive writing.

Medical research can result in new techniques, medicines or improved usage of existing technology leading to better patient care and outcomes.

We hope this issue will be a small step towards a new and improved Chettinad Health City Medical Journal. Please do give us your valuable feedback.

Dr. Sanjay Theodore,
Editor

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Commentary

Evolution of Surgical Coronary Revascularization

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Chettinad Health City Medical Journal 2015; 4(1): 2 - 5

Introduction

A heart attack in the 1950s was like a death warrant¹. Those who reached the hospital alive would be sentenced by the physician to be confined to bed for six weeks or longer and in spite of this 'treatment', nearly a third succumbed. Such devastating effects of Coronary artery disease stimulated physicians to look frantically for treatment. It was a challenging time for clinicians investigating treatment options for Angina Pectoris. Armed only with Electro Cardiograms - ECGs (recorded painstakingly on a drum or photographically to be developed in a dark room), the journey to understand the pathophysiology of Coronary Artery Disease and its treatment had just begun - with no Coronary Care Units, no echocardiography, no biological markers, no nuclear imaging, but just an infectious passion to contain the dreaded killer¹.

The pioneering work of Dr. Mason Sones in delineating the 'block' in epicardial coronary vessels through cine angiographies suggested that restoring blood supply to the affected territories would help. The routine use of the heart lung machine after Dr. John Gibbon corrected a congenital defect on 22 March 1955, gave surgeons the confidence to get involved in the search for treatment of a heart attack, a field monopolized hitherto only by physicians. Different surgical strategies were tried - endarterectomy, vein patch plasty and sutureless grafts to name a few. It was finally on 25 February 1964, that Dr. Vasilii Kolesov successfully anastomosed the Left Internal Mammary Artery to a coronary artery with fine sutures, effectively bypassing the coronary block - a technique that has been the mainstay of surgical coronary revascularization even today. This surgery has since been known as the Coronary Artery bypass Graft Surgery (CABG). The reversed saphenous vein, introduced as a conduit soon after, became the preferred choice due to the ease of harvesting. Thus Surgical Coronary Revascularization revolutionized treatment for Coronary Artery Disease^{2,3,4}. A new era in healthcare had begun.

With the tremendous success of CABG surgery in other countries, Indian surgeons who had trained in centers where this surgery was performed wondered about its feasibility in India. So, 11 years after Dr. Kolesov performed the historic surgery, India witnessed the first successful CABG by Dr. KM Cherian at Railway Hospital, Chennai in 1975. By the early 1980s, coronary

surgery was being performed in a handful of centers in Chennai, Mumbai, Delhi and Vellore (Table 1).

Corporatization of CABG

The burden of Rheumatic Heart Disease and Congenital Heart Diseases was so huge that CABG in teaching hospitals was not a priority. By the late 1980s many surgeons had returned from training abroad and most were absorbed into the private health care system with better infrastructure and remuneration. It was believed that coronary artery disease affects the more affluent strata of society, who could also afford the treatment. With this mindset, CABG was regarded as an 'elitist' operation.

This was not without reason. The 'corporatization' of CABG began with the establishment of the Apollo Hospital, Chennai in 1984 and the Escorts Hospital, Delhi in 1988. Mumbai became the hub of multispecialty private hospitals like Bombay Hospital, Breach Candy and Jaslok which catered to those who could afford this expensive surgery. Though a few teaching hospitals offered CABG, the vast majority of these surgeries were done in the private hospitals - using only reversed saphenous vein grafts for all the coronary vessels.

Many cardiac centers opened in the 90s and CABG surgery was being performed more frequently. Better infrastructure even in small centers lead to a boom in availability of tertiary care in the country. Considering it to be a matter of prestige, hospitals vied with each other to offer CABG surgery. Long term results of the CABG surgery indicated that the Left Internal Mammary Artery (LIMA) used on the Left Anterior Descending (LAD) artery was better in every way. By mid 1990, the standard surgery for Coronary Revascularization was the LIMA to the LAD and reversed saphenous vein as aorto-coronary grafts to the other vessels^{5,6}.

Sharing space

The 1990s witnessed an increase in the number of fixed cath labs from around 50 to nearly 150. As multiple imaging modalities became the mainstay in the diagnosis of structural heart disease, this meant more coronary imaging. A proliferation of ICUs ensured better care for patients of coronary disease with coronary angiography as an essential component. Importantly, it also

translated to an increase in patients referred for coronary surgeries. By the mid '90s, about 10,000 CABGs were performed in India annually. The accompanying dramatic rise in percutaneous coronary interventions in India prompted the National Intervention Council to maintain a national database of procedures.

Arterial Grafting

The global thrust on Arterial Revascularization at the turn of the century resulting from the knowledge of poor longevity of venous grafts was not lost on Indian surgeons. With better patency rates, this seemed to be the perfect answer to the younger Indian patients with limited resources looking for a 'one-time' solution of their coronary blockages. Encouraged by the long term results of the radial artery, a few surgeons started its routine use, in addition to the LIMA. The reported dismal patency of the radial artery forced a slump in its usage, but once it was clear that handling of the arterial conduit during harvesting, storage and deployment contributed to its behavior, there has been a resurgence in its use. There was a greater interest in 'Total Arterial Revascularization' (TAR) by the early part of the first decade of the new millennium. TAR was possible in most if not all of the patients, using limited arterial conduits by employing different strategies. Sequential anastomoses and pedicled grafts like the 'Y' graft – LIMA – RIMA, LIMA- Radial and the use of bilateral radial arteries became popular. The 'Y' graft also meant no manipulation of the aorta – a sound strategy to avoid neurological complications. Surgeons across the country started to use more arterial conduits.

Beating Heart Era

The first CABG performed by Dr. Kolesov was in fact on a beating heart without stabilizers. But the introduction of Cardiopulmonary Bypass and the still, bloodless field it provided, pushed beating heart surgery to the backburner. Though its revival began in the early 1970s, 'beating heart' CABG was done for the first time in India in 1992. The advent of stabilizing devices by the late 90s made it easier and 'Off Pump Coronary Artery Bypass' (OPCAB) caught the imagination of skilled Indian surgeons. Initially only the LAD, being anterior, was being grafted on a beating heart. With better techniques and an understanding of the need to position the heart differently before stabilizing it for anastomoses on other territories, multi vessel OPCAB gained more acceptance. It resulted in shorter ICU stay and promised to be more economical – important attributes in a resource-constrained country. A variety of stabilizers, intra coronary shunts and devices to assist proximal anastomoses helped the rapid rise in OPCAB procedures. It is estimated that now, more than 60% of the CABGs done in India are done on a beating heart. However, a note of caution has been expressed due to the recent discouraging reports of OPCAB and Indian surgeons need to justify this practice.

With the turn of the century, the dominance of surgeons as the main custodians of coronary revascularization also changed. More than 400 cath labs were installed by 2005 in India. Angiographies were being done on many more patients – even on those who

would have earlier been considered high risk. With tremendous improvement in imaging and hardware, Coronary Angioplasties with mainly Drug Eluting Stents were being performed on almost all types of lesions such as triple vessel, chronic total occlusions and left main disease. This change in the practice of Interventional Cardiology meant that mainly high risk patients were being referred for CABG – those with severe diffuse disease, with left ventricular dysfunction and with calcific vessels. OPCAB was logically a good option for these patients as it would avoid the deleterious effects of Cardio Pulmonary bypass. As experience with off pump techniques grew, results of OPCAB in patients with low ejection fraction, chronic kidney disease of various grades and even those with left main disease got better with each passing day.

Minimally Invasive Surgery

The Indian surgeon is restless! On the heels of beating heart surgery were further improvements. The natural progression seemed to be minimally invasive surgeries. So, 2 years after the introduction of OPCAB surgery, 'Minimally Invasive Direct Coronary Artery Bypass' (MIDCAB) involving the LIMA graft to the LAD through a left anterior thoracotomy in the 4th Inter Costal space, was done by Dr. Vivek Jawli in 1994. Preserving the shoulder girdle with a partial sternotomy has also been described, especially in obese patients. There is now a keen interest on sternal sparing surgeries spurred on by the success of minimally invasive surgery in multivessel disease. With better technology evolving for imaging and instrumentation, it promises to be the future of CABG.

Innovations in CABG surgery extended to harvesting techniques. Endoscopic vein harvesting avoids long scars on the legs especially in diabetics who have problems with wound healing. The radial artery has been harvested through a small incision with the use of a harmonic scalpel. Robotic coronary surgery has also been introduced in India, but its widespread use will be possible only when it makes better economic sense.

The unique Indian patient

Indian patients have smaller vessels with a more aggressive disease pattern. Hence endarterectomy was added to the armamentarium quite early in the Indian experience. Multiple skip grafts on the LAD to tackle such a diffuse disease has been advocated with good results. It must be noted that only minority of patients presenting for CABG are women. With smaller, fragile vessels and more comorbidities, they pose a challenge to the surgeon resulting in higher morbidity and mortality.

CABG for the masses

Coronary Artery Disease in India is of epidemic proportions. People of all strata of society – the rich, middle class and the poor are affected. It is alarming to note that younger patients, invariably the breadwinners suffer and unfortunately treatment costs cripple the family. Charitable hospitals offering free or subsidized treatment for such patients are few and not adequate for the vast majority of those afflicted. Fortunately this

is also changing. Government 'insurance' schemes and microfinancing schemes have been launched which make cardiac surgery – especially the much needed but expensive CABG surgery available to the masses. Over the last few years several state governments have made it possible for needy patients to undergo such treatment even in private hospitals. Reimbursements and insurance holders are on the rise and by keeping costs low, surgical revascularization has reached rural India. It is disturbing to note that there is widespread use of 'referral fees'. While trying to involve the primary medical practitioner, this route of questionable ethics, leads to the treatment becoming more expensive and threatens to derail the process of making tertiary cardiac care available to every Indian.

Future of CABG in India

Often patients presenting today for surgical coronary revascularization have already undergone a percutaneous procedure or have severe multi vessel disease. The challenge in today's times is to ensure that the overall morbidity and mortality of this surgery remains low with long lasting benefits in spite of sicker patients.

Surgical revascularization using the LIMA to the LAD has stood the test of time and is the gold standard of treatment for CAD. With an aging population and the high percentage of diabetics, the number of patients requiring CABG is escalating.

Because of the lack of a central surgical database, CABG numbers in the country and the pattern of its

practice are just estimates. It is believed that about 85,000 CABGs were performed in 2012, 92,000 in 2013 and more than 1,00,000 patients have undergone CABG in 2014. In comparison, Angioplasties saw a meteorological increase, nearly doubling, from 1,17,420 in 2010 to 2,16,817 in 2013, a growth of 23% . With around 2,48,000 angioplasties in 2014, the growth has now been pegged at 14%. Reading deeper into these statistics raises the question whether all options are presented to the patient at the time of treatment⁸.

Being the first point of contact to the patient, the primary physician and the cardiologist are the ones to recommend the treatment plan. Realizing that this is not an optimal practice, a 'heart team' approach has been emphasized the world over to ensure that the patient gets the best possible treatment – including the option of a hybrid procedure. It is in the interest of the medical fraternity in India to implement this expeditiously.

Surgical revascularization in India is practiced very differently from the west. Indian surgeons work with a difficult subset of patients and use beating heart techniques with arterial grafts. There has been a rise in the number of surgeries and the knowledge that these surgeons have to offer is immense. Establishing a national database is of paramount importance to start the process of analyzing this experience. Though India has lagged behind the West by about 10 years at the start of this era, there is no time lag today and in fact India has the potential to be in the lead.

Table 1 - Notable contributors to the evolution of CABG in India

K M Cherian	First CABG in India, Endarterectomy, OPCAB
Sharad Pandey	CABG in Mumbai
G B Parulkar	CABG in Government Teaching hospital (Mumbai)
P S Jairaj	CABG in Teaching Hospital (Vellore)
M R Girinath	CABG in corporate, Use of LIMA, Endarterectomy
P Venugopal	CABG in teaching Hospital, OPCAB, High risk CABG
S S Bhattacharya	TAR, LIMA-RIMA 'Y', OPCAB, High risk CABG, Endarterectomy, Re-do CABG
Naresh Trehan	CABG in Corporate, Arterial grafts, High Risk CABG, OPCAB, Minimally invasive, Robotic, Endoscopic
Vivek Jawli	1 st OPCAB in India, 1 st MIDCAB in India, LIMA-Radial 'Y', Arterial grafts, 1 st Awake CABG,
V V Bashi	BIMA use, OPCAB, High Risk CABG
Ramakant Panda	Radial artery use, TAR, OPCAB, High risk CABG, Re-do CABG
Devi Prasad Shetty	Insurance Microfinancing schemes, CABG to the masses, OPCAB, High Risk CABG
Yugal Mishra	OPCAB, Minimally Invasive, Arterial grafts, High Risk CABG, Robotic, Sternal sparing OPCAB
A Bhan	OPCAB, Radial artery use
Janardhan Reddy	OPCAB, partial sternotomy
Lokeshwar Rao Sajja	OPCAB, Bilateral MA, Radial Artery, CABG research
A. Gokhale	OPCAB, Sternal sparing CABG
T. Roy Chaudhary	OPCAB, Sternal sparing CABG
Murali Vettath	OPCAB, Proximal anastomotic obturator
Sanjeeth Peter	TAR, BIMA, Bilateral Radial use, OPCAB, High Risk CABG,

Surgical Coronary Revascularization - at a turning point

CABG with arterial grafts has gained popularity and will be the mainstay of treatment for multivessel and complex coronary artery disease. To stay relevant and be the treatment of choice, surgeons have to ensure that in addition to providing long term benefits, the technique of surgical revascularization is associated with a short period of recuperation thus allowing patients to return to regular work quickly.

We are at the cross roads of Surgical Coronary Revascularization. The path we choose will shape the future not just of coronary revascularization, but also of the specialty. This has the ability to rekindle the waning interest among young surgeons. Focusing on (i) sternal sparing arterial revascularization with fast recuperation and minimal morbidity, (ii) joining hands to form a heart team and (iii) establishing an accurate real time database is the route to take. With this, Indian surgeons are capable of being at the forefront of coronary revascularization in research, technique and training. The journey of Surgical Coronary Revascularization promises to be challenging, thrilling and rewarding.

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Women and Alzheimer's

Nearly two-thirds of persons with Alzheimer's disease are women. The usual explanation given is that the women on an average live 4-5 years longer; this longevity predisposes them to pre-senile dementia. Although age is considered to be the single most important risk factor, other as yet undefined factors may be at play. A recent estimate suggests that at the age of 65, a woman has 1 in 6 chance of developing Alzheimer's during the rest of her life; while in man that risk is 1 in 11!. Besides, after Alzheimer sets in, it progresses much faster in women than in men. But gene research provides most compelling evidence of a sex difference. Researchers from Stanford University analysed the gene associated with increased risk for Alzheimer's - ApoE-4 - in 8000 individuals. In women, this gene doubled the risk while in men, the increase in risk was only marginal. The increased susceptibility of women may be related to the nature of interaction of this gene with oestrogen.

- Dr. K. Ramesh Rao

Perspective Article

Personalized Medicine

Pitchappan RM*

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Prof. Ramasamy Pitchappan Ph.D., Fellow of the Indian Academy of Medical Sciences and Indian Academy of Sciences, is the Director of Research at Chettinad Academy of Research & Education, since 2010. With forty years of research experience in the field of Immunology of infectious diseases, Immunogenetics, Genetic epidemiology and Human Genomics, he served and retired as Chairperson, Professor & HOD of Immunology and School Biological sciences at Madurai Kamaraj University. He also served as Directors of Science Education Centre and Educational Media Research Centre and also carried out 'The Genographic Project', India, funded by NGS-IBM and Ted Waitt Family foundation, USA. His seminal findings with international

collaborators were deciphering the genome predisposing for leprosy, HLA DR2 association in tuberculosis immunity and the first coastal migration of Man from Africa to Australia through India and peopling of Tamil Nadu and India. A pioneer in transplantation immunology and immunology of infectious diseases established HLA Tissue matching laboratory at MKU in 80s and offered kidney and bone marrow transplantation services for >3,000 end stage renal failure and bone marrow transplantation families. He is a member of various scientific & governmental bodies regulating science and policies in India. He is the author of more than 100 original scientific publications with a H index of 20.

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Chettinad Health City Medical Journal 2015; 4(1): 6 - 7

Introduction

'Genetics' is a term 'allergic' to most of the physicians, but the day has come that they need to understand and make use of it for better patient management. There are many studies in recent times showing unequivocal association of select genes with hypersensitivity to select drugs. One such widely known in the recent times is the 'Abacavir', an anti-retroviral drug widely used to treat AIDS patients, and patients with HLA-B*57:01 develop severe adverse reactions¹. Another sister clade of this HLA, viz B*58:01 has on the other hand been shown to cause severe cutaneous adverse reactions (SCAR) with 'allopurinol' treatment of gout patients². Hence in the West, clinics have started testing HLA B*57 and 58 status before prescribing these drugs.

This has great relevance to India in practicing medicine and avoiding such unwarranted outcomes. It is known that HIV infected patients with HLA B*57 normally turn into long term non progressors (LTNP) and in India too these patients show good CD4 count and may stay healthy for long without progressing towards AIDS. Our study on Bangalore cohorts is the tip of the iceberg³. HLA B17, particularly its split, B*57 (revised nomenclature HLA B*57) is one of the common alleles in India (Fig 1) to be called as Telugu haplotype by Brian Hamman from Durban, South Africa, as early as 1979⁴. Interestingly this allele and its haplotype HLA A1-B17 is present only in certain populations of India and not all; again not in all demes (populations, castes) of a state.

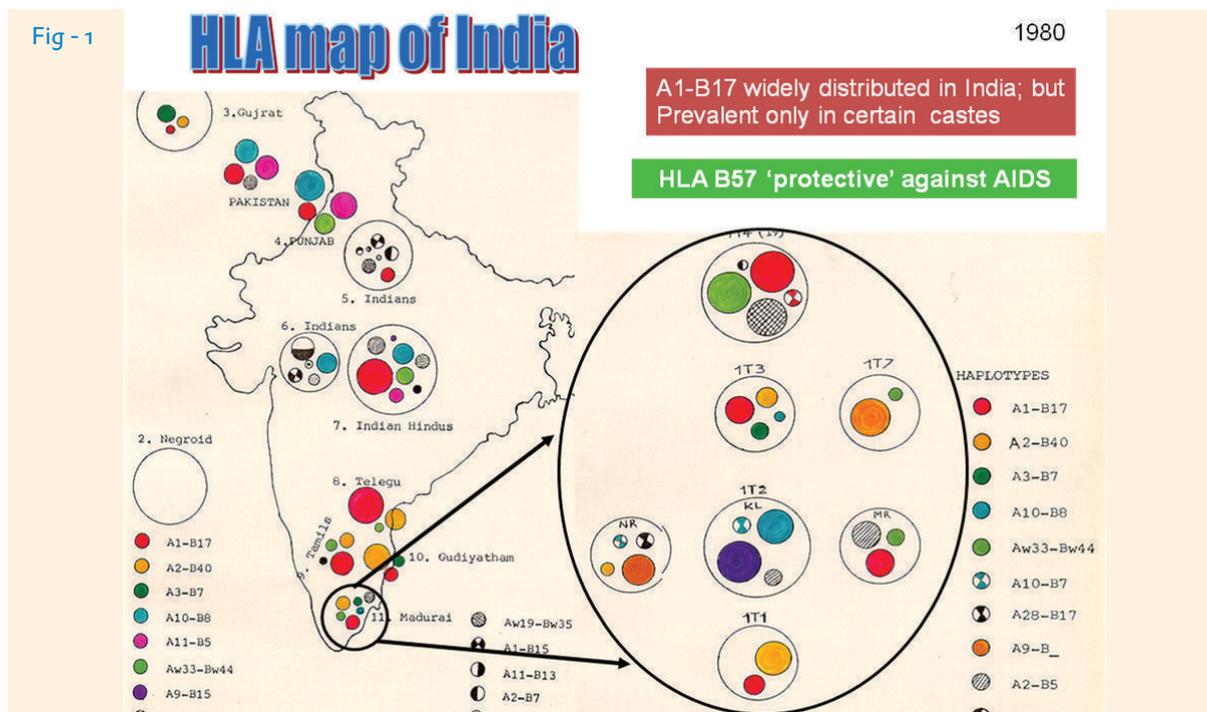


Fig 1 - HLA A-B haplotypes identified in various studies on different populations of India are mapped in the respective regions sampled. Each color represents one haplotype and the relative size, their frequencies. Larger the dot, higher the frequencies. Data were all from literature and from our lab as of 1980.

Note that while some colors are strewn all over, not all are distributed widely. The samples from Madurai, ~540, in 1980 were stratified based on social ladder, major population groups / castes (inset). Observe how distinct and disparate they are from one another. Note particularly the red dots: it is HLA A1-B17 haplotype. HLA B17 has two splits 57 and 58, of which 57 is prevalent in Indian populations studied so far. Thus B17 though present in many populations considered, they differ in their frequencies and not present in many other populations.

HLA B17(57) positive HIV seropositives possess normal CD4 count (>400) and they do not progress towards AIDS faster. Hence they will survive in population for longer, thus infecting more partners. This epidemiological scenario warrants to understand the immunogenetic basis of LTNP (<10,000 viral count) and elite controllers (<50 viral count) in India and to undertake appropriate strategy in HIV control.

(Nostalgic memories: The HLA A-B haplotype India color map, was made by Pitchappan in 1980 for Prof. Dausset, the Nobel laureate, discoverer of the HLA system for his presentation, during one of his (Pitchappan) visits to France.: At that time, the significance of HLA B17 was not known to anybody!)

Alas, no systematic study on Immunogenetic profiling of Indian populations has been carried out, sans the piecemeal publications by a handful of groups in India. Hence time is ripe that a systematic study on 'immunogenome' of Indian population is undertaken and further, this kind of gene diagnostic tools⁵ are put to use in India for better patient management.

It is disturbing to note that 'Penicillin, called the wonder drug that saved tens of thousands (12-15%) of patients in World War II, shunned in India by medical practitioners. About 6% of Caucasians administered with this drug developed serious symptoms that required attention of an allergologist, while Asians are not susceptible to this allergy (Albin & Agarwal, 2014)⁶. In a genome wide fine mapping analysis, HLA-DRA rs7192 and rs8084 have been shown to be associated with allergy to penicillins and amoxicillin but not to cephalosporins (Guent et al 2015)⁷. In resource poor countries such as India, one has to look at cost benefit ratio of the available drugs and use the meager resources more effectively to alleviate the sufferings of the poor. Whether to use a broom stick or a nuclear missile to kill a cockroach at home is the question. One has to practice evidence based and pragmatic medicine, and spare the sophisticated antibiotics for emergencies. Time is ripe in India for practitioners and policy makers to think and act in the right direction, and to practice appropriate, evidence based, predictive medicine.

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Original Article

Minimally Invasive Aortic Valve Replacement Does Not Reduce the Incidence of Postoperative Atrial Fibrillation

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Abstract

Objective: Due to an aging population needing aortic valve replacements (AVR), there is a growing need for minimally invasive cardiac surgery aimed at reducing operative trauma and peri-operative morbidity. Large case series have reported minimally invasive (MI) AVR to be a good alternative to median sternotomy AVR with faster recovery and reduced morbidity. Our aim is to review our early experiences with MI AVR and compared that to full sternotomy (FS) AVR.

Methods: We performed 35 cases of MI AVR and 62 cases of FS AVR from January 2012 to September 2014. Prospectively collected perioperative data was analysed retrospectively. MI AVR consisted of 7 right anterior thoracotomy and 28 partial sternotomy cases. All patients were followed up in accordance with the Australian and New Zealand Society of Cardiac and Thoracic Surgeons (ANZSCTS) database requirements.

Results: The mean age for FS and MI was 70 and 69 years respectively. FS cohort had a shorter mean cardiopulmonary bypass time (86 vs. 104 minutes; $p=0.003$) and aortic cross clamp time (70 vs. 84; $p=0.002$). Mean ventilation time favoured the MI group at 8.6 hours compared to 12 for the FS group ($p=0.034$). MI patients trended towards less postoperative inotrope requirements, lower postoperative creatinine, and lower postoperative atrial fibrillation rates. There have been no wound breakdowns to date. There were no operative mortalities.

Conclusion: MI AVR can be performed safely and with equivocal results compared with FS AVR. MI AVR is a good alternative to the traditional median sternotomy approach with potential for improved post-operative recovery.

Key Words: Aortic Valve Replacement, Minimally invasive

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Introduction

In the western world, the commonest acquired heart valve disease is Aortic stenosis (AS). It is generally a result of a myriad of degenerative changes associated with native annular and leaflet calcification. The Gold Standard for treatment of AS remains a surgical aortic valve replacement (AVR). Prior to the first report of minimally invasive (MI) cardiac surgery for AVR in the 1993 by Rao et al¹, all AVR procedures were performed via a median sternotomy with direct arterial cannulation of the distal ascending aorta and right atrial venous cannulation for cardiopulmonary bypass (CPB). Enthusiasm and popularity for MI AVR grew in the late 1990s as an alternative to a traditional full sternotomy (FS) for patients with isolated aortic valve disease. Various techniques have been described including: parasternal, infra-axillary, lower hemi-sternotomy, transverse sternotomy, upper hemi-sternotomy, and right anterior thoracotomy. Today, the vast majority of

MI AVR cases globally are performed using either an upper partial sternotomy extending into the 2nd, 3rd, or 4th intercostal spaces (referred to as a "J", "L", or inverted "T") or a right anterior (parasternal) thoracotomy (RAT) at the 2nd intercostal space²⁻⁵.

Benefits of MI AVR, which include improved cosmesis, reduced pain, reduced surgical trauma, reduced blood loss, reduced transfusion requirements, shorter ventilation times, earlier functional recovery, shorter ICU and inpatient hospital stay, have been shown in numerous reports⁶⁻⁹. As such, many large cardiac surgical institutions have adopted MI AVR as the preferred approach for all isolated AVR procedures. As experience in MI AVR has developed over the past decade, there are growing reports of extending the scope of MI AVR to include redo patients, concomitant mitral and/or tricuspid valve, or aortic procedures^{10,11}. Despite this, widespread acceptance of MI AVR has been slow in Australia. There are concerns of increased

CPB and aortic cross-clamp times due to limited access, which are predictive of worse outcomes in cardiac surgery. Other concerns include the significant learning curve required to adopt a new surgical technique and uncertainty in the "real world" benefits of MI techniques.

In this paper, we report outcomes of MI AVR cases performed at our institution from January 2012 to September 2014 and compare that to conventional FS AVR cases during this same time period.

Methods

This is a retrospective observational cohort study of all isolated aortic valve replacement procedures. Data is collected prospectively for all patients undergoing cardiac surgery at our institution in accordance with the Australian and New Zealand Society of Cardiac and Thoracic Surgery (ANZSCTS) database. Follow-up is obtained by phone call at 30 days after the date of operation.

All AVR cases from January 2012 to September 2014 were identified from our database retrospectively. Cases where concomitant procedures such as coronary artery bypass grafting, mitral or other valve surgery, replacement of the ascending aorta, or atrial fibrillation ablation had been performed were excluded for analysis. Patients who had previous surgery or had a history of postoperative atrial fibrillation were also excluded from the analysis.

Surgical Technique

Partial Sternotomy (PS)

We used an upper partial sternotomy from the jugular notch through a 7-9 cm skin incision. The sternum was divided in the midline and subsequently transected horizontally into the 2nd to 4th intercostal spaces, either unilaterally to the right or bilaterally. The right internal mammary artery was divided if necessary. Thymic fat was dissected as via FS, pericardiectomy performed and pericardial sutures are placed and retracted. The patient was fully heparinized and the ascending aorta was palpated for safe cannulation sites. Venous drainage was achieved with either venous cannula inserted into the right atrial appendage or by inserting a long multi-stage right atrial venous cannula through the right femoral vein. Cardiopulmonary bypass was initiated and the aorta was directly cross-clamped. Antegrade and retrograde cold blood cardioplegia was given and, if aortic insufficiency is present, direct ostial cardioplegia was given after performing the aortotomy.

Right Anterior Thoracotomy (RAT)

We created a 5 cm parasternal incision over the 2nd or 3rd intercostal space and entered the pleural cavity. The costalchondral cartilage may be divided at the sternal edge to allow a larger operative field. The pericardiectomy was performed, sutures placed, and pericardium is retracted. The patient was fully heparinized and was then cannulated via the femoral artery and veins with continuous guidance with Transoesophageal echocardiography. Cardiopulmonary bypass was

initiated, the aorta was then clamped and antegrade cold blood cardioplegia is given. If aortic insufficiency was of concern, direct ostial cardioplegia was given after performing the aortotomy.

Patient Selection

The decision of whether patients undergoes a MI AVR or a FS was at the sole decision of the surgeon and patient. We performed an additional non-contrast CT scan for patients who are being considered for a RAT approach.

Statistical Analysis

Categorical variables were analysed using chi-squared or fisher exact tests where appropriate. Continuous variables were conducted using a t-test and are presented as means \pm standard error of the mean (SEM) or medians and inter-quartile ranges as appropriate. All analyses were performed using STATA v13.1.

Results

We identified 97 AVR cases that matched our criteria for this analysis. There were 62 AVR cases performed via a full sternotomy (FS) and 35 performed with a minimally invasive (MI) approach. The MI AVR cases were comprised of 28 PS and 7 RAT. Preoperative characteristics for the FS and MI cohorts were generally well balanced for heterogeneity as shown in Table 1. The only baseline characteristic that was statistically significant was BMI where the MI group had a mean BMI of 22 kg/m² as compared with 32 kg/m² for the FS group ($P=0.013$). The MI group had a higher proportion of males (71% vs. 52%), however this was not statistically significant.

The mean age for the FS and MI AVR groups were 70 and 69, respectively. Infective Endocarditis represented 8% of patients in the FS group but none in the MI group. In addition, the FS group had a higher proportion of peripheral vascular disease (8% vs. 3%), previous cerebrovascular accident (5% vs. 0%), lung disease (13% vs. 6%), and patients with a NYHA class of 3 or 4 (34% vs. 20%). Preoperative diabetes, hypercholesterolemia, eGFR and BSA were all well balanced between the 2 cohorts.

Mean intraoperative cardiopulmonary bypass times in the FS and MI groups were 86 and 104 minutes, respectively ($p=0.003$). Similarly mean cross clamp times for FS and MI cohorts were 70 and 84 minutes ($p=0.002$), respectively, shown in Table 2. Only 1 patient required an intra-aortic balloon pump, which was in the FS group. In the intensive care unit, patients in the MI group were significantly quicker to wean off ventilation with a mean ventilation time of 8.6 hours compared to FS where mean ventilation was 12 hours ($p=0.034$). Although it was not statistically significant, mean ICU length of stay was also shorter in the MI group compared to the FS group, being 28 hours and 41 hours respectively ($p=0.187$). In addition, MI group had a slightly reduced incidence of red blood cell and non-red blood cell products transfusion. However, drainage output were significantly higher in the MI group with average 4-hour drainage output of 217 ml compared with 146 ml in the FS group ($p=0.047$). Three patients were required to return to theatre for

bleeding, comprising of 2 in the FS group and 1 in the MI group. MI patients showed lower incidence of inotrope use of more than 4 hours for low cardiac output compared at 11% compared to 27% for FS patients (p=0.066). Similarly, other postoperative outcomes were also not statistically different between

the FS and MI group (Table 3). However, there was a trend towards lower postoperative creatinine in the MI group (mean: 105 $\mu\text{mol/L}$ vs. 126 $\mu\text{mol/L}$). The incidence of postoperative atrial fibrillation was 37% in the FS and slightly less at 29% in the MI group, however this was not statistically significant (p=0.395).

Table 1 : Baseline characteristics

Baseline Characteristics	FS (n=62)	MI (n=35)	P value (\leq)
Age (years)	70 \pm 1.4	69 \pm 1.8	0.848
Male sex	32	25	0.057
Smoking (current)	38 (5)	24 (7)	0.473 (0.086)
Family History of CAD	21	9	0.629
Diabetes	14	9	0.727
Hypercholesterolemia	30	19	0.577
CVD	3	0	0.186
PVD	5	1	0.307
Lung Disease	8	2	0.263
Infective Endocarditis	5	0	0.085
Heart Failure (at time of surgery)	11 (4)	7 (1)	0.784 (0.442)
HYHA 3 or 4	21	7	0.148
eGFR (ml/kg/min)	85 \pm 4.7	80 \pm 5.7	0.556
Preoperative Creatinine($\mu\text{mol/L}$)	92 \pm 4.3	92 \pm 4.9	0.999
BMI (kg/m ²)	32 \pm 0.84	28 \pm 1.0	0.013
BSA (m ²)	1.94 \pm 0.028	1.93 \pm 0.043	

Continuous variables are reported as mean \pm stand error of the mean (SEM) and discrete/categorical variables are reported as whole numbers where statistically significant results are those with p<0.05

FS = Full sternotomy; MI = Minimally Invasive; BMI = Body mass index; BSA = Body surface area; CVD = Cerebrovascular disease; PVD = Peripheral vascular disease; CAD = Coronary artery disease; HYHA = New York Heart Association; eGFR = estimated Glomerular Filtration Rate

Table 2 : Intraoperative & ICU Characteristics

Intraoperative & ICU Characteristics	FS (n=62)	MI (n=35)	P value (\leq)
Cardiopulmonary Bypass Time (minutes)	86 \pm 3.0	104 \pm 5.3	0.003
Cross Clamp Time (minutes)	70 \pm 2.5	84 \pm 4.4	0.002
ICU stay (hours)	41 \pm 7.1	28 \pm 3.6	0.187
Ventilation (hours)	12 \pm 1.1	8.6 \pm 0.96	0.034
Prolonged ventilation > 24 hours	6	1	0.213
4-hour drain output	146 \pm 17	217 \pm 20	0.470
Red Blood Cell Transfusion (incidence)	16	5	0.186
Non-Red Blood Cell Transfusion (incidence)	13	9	0.592
Return to Operating Theatre	2	1	0.920
Re-intubation	1	1	0.679
Perioperative Cardiogenic Shock	1	0	0.450
Inotropes longer than 4 hours post-op	20	8	0.326
- For low cardiac output	17	4	0.066
- For low SVR	13	6	0.649
IABP requirement	1	0	0.570

Continuous variables are reported as mean \pm stand error of the mean (SEM) and discrete/categorical variables are reported as whole numbers where statistically significant results are those with p<0.05

FS = Full sternotomy; MI = Minimally Invasive; ICU = Intensive care unit; IABP = Intra-aortic Balloon Pump

Table 3 : Postoperative Outcomes

Postoperative Outcomes	FS (n=62)	MI (n=35)	P value (\leq)
New renal failure	3	1	0.637
- Dialysis	3	1	0.637
- Post-operative Creatinine (umol/L)	126 \pm 7.1	108 \pm 4.2	0.077
New PPM requirement	5	2	0.885
Cardiac Arrest	1	0	0.450
CVA/TIA	0	0	-
Pulmonary Embolism	0	1	0.181
Pneumonia	1	0	0.450
Deep sternal wound infection	0	0	-
Post-operative Atrial Fibrillation	23	10	0.395
Postoperative length of stay (days)	7.7 \pm 0.6	6.8 \pm 0.3	0.168
Readmission	3	3	0.440
Mortality at 30 days	1	1	0.637

Continuous variables are reported as mean \pm stand error of the mean (SEM) and discrete/categorical variables are reported as whole numbers where statistically significant results are those with $p < 0.05$

FS = Full sternotomy; MI = Minimally Invasive; SVR = Systemic vascular resistance; CVA = Cerebrovascular accident; TIA = Transient ischaemic attack;

Discussion

Minimally invasive cardiac surgery represents a significant change in the approach to traditional procedures. Benefits of MI AVR have been reported widely after increasing popularity in the past decade. This is often without increases in mortality or serious morbidity. Despite this, skepticism of MI techniques remains and some require further evidence of reported benefits.

We have described a local experience after introducing MI AVR techniques with the associated learning curve at a regional tertiary cardiac referral centre in Australia. Although our series is small in comparison to many European and North American reports, our progression through the MI learning curve is undoubtedly comparable¹².

The major finding of our study is a reduction in ventilation time, which has essentially been a universal result from contemporary papers in MI AVR. This has been widely attributed to reduced postoperative pain resulting in faster recovery in breathing mechanics and mobilization. We also noticed trends in reduced ICU length of stay, and RBC transfusion rates in MI AVR patients, although these did not achieve statistical significance, most likely due to a small sample have also reported reduced RBC transfusion rates base on the principle of reduced dissection in MICS leading to less bleeding.

Our MI cases resulted in longer cardiopulmonary bypass and cross-clamp times when compared with the FS counterparts. This is most likely due to restricted access and increased surgeon caution present for all new techniques. Specifically for our cohort, the majority of MI patients would have been part of the learning curve inherent in all new procedures. Our results are consistent with current literature, albeit a much smaller series of MI AVR cases^{3,4,13,14}.

It was surprising that we did not show a trend towards reducing POAF, which had been reported other

series¹⁵. However, a recent meta-analysis by Phan et al also did not yield a difference in POAF between FS and MI AVR cases¹⁶. Postoperative atrial fibrillation is a complex multifactorial entity, however studies showing reduced POAF rates is certainly based on improvements on other patients' perioperative parameters. Although we have not seen differences in POAF rates, as the most common adverse event after cardiac surgery, it is a potential for additional benefits of MI AVR.

Partial sternotomy offers the surgeon with a familiar view and access, albeit smaller, and almost universally regarded as a technique with an easier learning curve when compared with a RAT. In addition, there are no further investigations necessary for patient selection with PS MI AVR.

From our experience to date, we believe a PS access is a safe approach to the introduction of MI AVR to a cardiac surgical unit. With increased experience and familiarity with MI access, RAT can be introduced safely and seamlessly.

Study Limitations

This study is subject to all the limitations of a single center experience retrospective observational cohort study. Relatively small numbers of our study may bring into question its generalizability. Reported cases are inclusive of all our MI AVR experience and include cases which were part of our learning curve. Therefore, our results may underestimate the benefits of MI AVR, which larger series and meta-analysis have shown.

Conclusion

MI AVR is more technically demanding when compared with traditional sternotomy AVR, especially during the initial learning curve. Despite this learning curve MI AVR via a partial sternotomy or RAT can be performed safely and effectively. Peri-operative outcomes in these patients are at least similar to FS AVR. MI AVR is becoming increasingly accepted and

with our aging population. MI AVR should be considered for all patients requiring an AVR.

The authors declare no conflict of interest.

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Original Article

Does Combined Antegrade and Retrograde Cardioplegia Offer Better Myocardial Protection in Patients Undergoing Valve Surgery?

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Abstract

Objective: Myocardial ischemia is metabolic phenomenon that occurs in patients undergoing open heart surgery like Coronary Artery Bypass Grafting and Valve surgery due to interruption of coronary blood flow during aortic cross-clamp and reperfusion after aortic cross-clamp release. This myocardial damage leads to hemodynamic instability, arrhythmias, high dose of inotropes, difficulty in weaning of CPB and chance of intra aortic balloon pump use. This study examined the efficacy and safety of Retrograde with Antegrade Cardioplegia comparison with Antegrade approach in valve surgery.

Methods: The effects of Retrograde with Antegrade (ACP+RCP) and Antegrade (ACP) delivery of Cardioplegia were evaluated and compared in 30 patients. The patients were randomly separated into 2 groups, Group -1-ACP+RCP (n=15), Group -2-ACP (n=15). Cardiac energy metabolism was monitored by evaluation of coronary sinus lactate levels. Blood samples were taken from Coronary Sinus during soon after cannulation, before institution of CPB and on removal of aortic cross-clamp.

Results: There was an increase of the coronary sinus lactate levels during aortic cross-clamp period in both groups. The rise in lactate levels was lower in the group-1 than group-2.

Conclusion: Based on this study we conclude that combined antegrade and retrograde cardioplegia provides good myocardial preservation and may provide superior preservation in case of long clamp times and extensive surgeries.

Key Words: Cardiopulmonary bypass, Antegrade cardioplegia, Retrograde cardioplegia, Lactate, Myocardium.

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Introduction

Myocardial ischemia is a metabolic phenomenon that occurs in patients undergoing open heart surgery like coronary artery bypass grafting and valve surgeries¹. This happens due to stress response to Cardiopulmonary bypass (CPB) and interruption of coronary blood flow during aortic cross clamp and reperfusion after aortic cross clamp release¹.

During cardiac surgery, myocardial damage is cumulative. Cardiac surgery at some point will induce ischemia to myocardium. Each patient's myocardium will respond differently and lead to immediate or delayed poor outcome. This myocardial damage leads to hemodynamic instability, arrhythmias, high dose of inotropes, difficulty in weaning of CPB and chance of intra- aortic balloon pump use.

Hyperlactatemia occurs in anaerobic conditions where induced glycolysis occurs with the stimulation of exo and endogenous catecholamines. Once anaerobic conditions prevail, pyruvate a substrate for oxidative

phosphorylation cannot be utilized. Therefore the level increases and it is diverted to the formation of lactate. Normal lactate to pyruvate ratio i.e. LP ratio is 10:1 which also occurs in the cases of increased metabolism, but increases in LP ratio >10:1 occurs in tissue hypoxia alone¹.

Cardiac metabolism is monitored by evaluation of coronary sinus (CS) lactate concentration and we hypothesized that myocardial lactate levels can be used as markers of myocardial dysfunction during and after cardiopulmonary bypass. We sought to evaluate efficacy and safety of Antegrade with Retrograde (RCP) in comparison with only Antegrade (ACP) approach in valve surgery.

Materials and Methods

This clinical observational study was conducted in Department of Cardio-thoracic surgery, Chettinad Health City, Chennai. Thirty patients who underwent elective valve surgery with CPB were included in this study (Table-1).

RCP and ACP delivery of cardioplegia were evaluated and compared in 30 patients, and randomly separated in 2 groups, Group -1-ACP+RCP (n=15), Group -2- ACP (n=15).

Patients with neurological dysfunction, hemodynamic instability, coagulopathy, aneurysm, congestive heart failure, redo surgery and emergency surgeries were excluded from this study.

Operation Technique

All patients underwent valve surgery with a standard CPB protocol under moderate hypothermia at 30-32 degree Celsius. Pump flow rate and perfusion pressure were maintained at 2.2-2.6 l/min/m² and 50-80 mmHg, respectively. Alpha stat-strategy was used for blood gas management and blood sugar was maintained between 100 and 200 mg/dl during CPB. A hematocrit of 18-27% and mixed venous oxygen saturation of 70-75% was maintained.

Myocardial protection was achieved with intermittent blood cardioplegia St Thomas solution, 4:1, (4 parts of oxygenated blood and one part of crystalloid solution). Cardioplegia (CP) was delivered through Spictra myocardial protection system, repeated at 20-25 min intervals. CP solution was cooled and maintained at 20°C - 25°C. In both groups cardiac arrest was achieved with an Antegrade infusion into aortic root at pressure of 80-100 mmHg with HK (high concentrated potassium 20mEq/l). After initial dose of Antegrade cardioplegia infusion, the aortic root was vented and retrograde cardioplegia delivery with LK (low concentrated potassium 10mEq/l) was infused into the coronary sinus cannula (DLP manual inflating cuff 15 Fr, Medtronic, Inc. Minneapolis, MIN, USA). Retrograde cardioplegia delivery pressure was monitored by a separate monitoring line and was maintained between 35-45 mmHg.

Blood samples were collected from coronary sinus (CS) through Retrograde CP cannula² (Fig. 1) and myocardial lactate levels were measured by commercial gas analyzer (ABL 800 basic).

Sampling Methods

1. Soon after cannulation, before institution of cardio pulmonary bypass.
2. On removal of aortic cross clamp

The intraoperative variable records included CPB time and aortic cross clamp time. The postoperative variables observed included post-CPB need for inotropes, duration of mechanical ventilation, inotrope usage and ICU stay.

Statistical Methods

Statistical analysis was performed with Social Science Statistics (SSS). Descriptive analysis and paired t-test were used for comparison between the groups. A p-value less than 0.05 was considered statistically significant. Data is presented as mean ± standard deviation where appropriate.

Results

Patients were randomly divided into 2 groups Group-1 ACP+ RCP and Group-2 ACP. Patient characteristics were comparable in both groups (Table-2). CPB time, aortic cross clamp time was significantly higher in RCP group but there was no difference in myocardial lactate levels in both groups (Table 3). Duration of mechanical ventilation and length of ICU stay were similar in both groups (Table 3).

Coronary sinus lactate levels during cross clamp period were high in both groups, comparatively. Group-1 lactate levels were lesser than Group-2. Differences in coronary sinus lactate levels were not significant (Table 4).

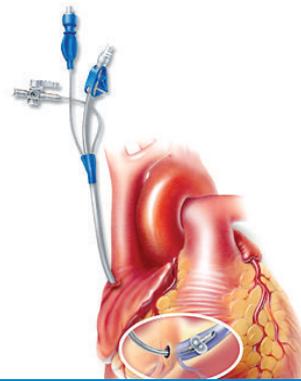


Fig 1 - Retrograde cardioplegia cannula

Table 1 - Operating Procedures

Valve Procedures	Group-1	Group-2
MV repair	1	2
MVR	5	8
AVR	3	0
DVR	5	4
MVR+ASD	0	1
OMV	1	0

Table 2 - Patient Demographics

Patient Demographics	Group-1 (n=15)	Group-2 (n=15)	p-value
Age	46.8±13.42	41.4±12.98	0.23
Age>60	2	0	0.16
Sex(M/F)	11/4	5/10	-
NYHA(II/III/IV)	2/9/4	1/10/4	0.77
Single valve	10	11	0.33
Double valve	5	4	0.5
LV Function <60%	3	5	0.33
PA Pressure>60%	2	1	0.33

p value <0.05 significant

Table 3 - Operative and Post Operative Variables

Operative and Post Operative variables	Group-1 (n=15)	Group-2 (n=15)	p-value
CPB time	74.33±26.52	58.4±18.98	0.068
X-clamp time	53.93±12.89	41.86±15.25	0.02
Mechanical ventilation(minutes)	172±48.43	183.4±34.64	0.30
ICU stay(Hours)	40.6±4.41	40.4±4.29	0.91
Ventilation > 24 Hrs	0	0	-
Inotropes > 24Hrs	2	1	0.33

Table 4 - Coronary Sinus Lactate Levels

Coronary Sinus Lactate	Group-1	Group-2	p-value
Pre-bypass	0.853	1.2	0.16
Post clamp	2.78	3.48	0.49

p value <0.05 significant

Discussion

Improvements in myocardial protection have contributed to improved results after cardiac surgeries. Better myocardial protection will decrease the morbidity and mortality². Optimal myocardial protection requires uniform delivery of cardioplegic solution throughout the heart³. The infusion of cardioplegia solution through the aortic root is a common delivery method used by the majority of cardiac surgeons. This method produces rapid diastolic arrest and good preservation of myocardial function, but in patients with aortic insufficiency and during LA retraction this approach can result in uneven and inadequate distribution of cardioplegia solution to the myocardium. This limitation of antegrade cardioplegia can be overcome by using of coronary sinus retrograde cardioplegia³. Retrograde cardioplegia has several advantages including. 1. Exclusion of need for aortotomy and coronary ostial cannulation in patients with minimal aortic insufficiency. 2. Homogenous distribution of cardioplegia. 3. Avoidance of direct coronary cannulation and possible late ostial stenosis and uneven cooling of myocardium⁴. Disadvantages of retrograde cardioplegia include possible barotrauma, chances of coronary sinus rupture, myocardial oedema and inadequate right ventricular preservation³. Generally retrograde cardioplegia administration requires more time to deliver same amount of Antegrade CP solution, because of lower flow rates (100-200 ml/min) and pressures (35-45 mmHg) to prevent myocardial oedema and coronary sinus injury³. Group-1 received first dose of cardioplegia solution through Antegrade route, after achieving cardiac arrest with initial Antegrade infusion, the aortic root was vented and Retrograde cardioplegia was delivered through coronary sinus cannula.

Loop and associates, compared Antegrade and combined Antegrade +Retrograde blood cardioplegia⁵. They found that combined group showed decrease in the levels of morbidity, mortality and cost, comparatively more in antegrade cardioplegia alone⁵. Bhayana et al. reported the results of combined delivery and antegrade alone⁶. The results suggested the antegrade cardiac arrest followed by retrograde infusion may be responsible for more rapid recovery of left ventricular stroke work index and may provide superior myocardial protection. Diehl's group evaluated and found that the group that received combined delivery had improvements in radionuclide derived left ventricular ejection fraction, and overall myocardial performance, mortality were unchanged in both groups⁷. The sampling of coronary sinus blood via cannula in coronary sinus is a simple, cheap, easy technique and can be performed routinely. Myocardial lactate levels may be effective in predicting post operative needs for inotropes, post operative myocardial dysfunction, duration of post operative ventilation and ICU stay. Retrograde cardioplegia in

combination with Antegrade cardioplegia has been demonstrated to be an effective and safe technique for myocardial preservation; clinical outcomes does not appear to be affected by the route of cardioplegia administration^{8,9}.

Conclusion

We conclude that combined antegrade and retrograde cardioplegia provides good myocardial preservation and may provide superior preservation in case of long clamp times and extensive surgeries. Clinical benefit may become more apparent with larger number of patients.

Authors declare no conflict of interest.

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Original Article

Risk Factors for Coronary Artery Disease in a Semi-urban area of Tamil Nadu

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Abstract

Background : Coronary artery disease (CAD) is the most common cause of mortality in India with 3 million deaths annually. Deaths occurring due to CAD occur 5–10 years earlier in the Indian subcontinent than in Western countries. We studied the risk factors in a semi-urban area of Tamil Nadu with special reference to the conventional risk factors like diabetes, hypertension, hypercholesterolemia, smoking, and family history of coronary artery disease and other modifiable risk factors.

Methods : This study was a prospective and case controlled study where 50 patients with coronary artery disease and 50 control samples were studied.

Inclusion criteria included a positive treadmill test and/or angiographically proven coronary artery disease. A questionnaire in English and Tamil, was given to all patients diagnosed with coronary artery disease. Age, sex, diabetes, hypertension, hypercholesterolemia, smoking, family history of coronary artery disease, alcoholism, obesity and exercise levels were assessed.

Results & Conclusion : CAD was associated with diabetes and hypertension though not statistically significant. Hypercholesterolemia, smoking, family history of CAD, alcoholism, obesity and lack of exercise played a statistically significant role in CAD.

Key Words: Epidemiology, Coronary artery disease

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Introduction

Coronary artery disease (CAD) is the most common cause of mortality in India with 3 million deaths annually. India has 29.8 million symptomatic patients with CAD, 19.3 million diabetics and 118 million hypertensive individuals, who are at risk of developing metabolic syndrome, thus increasing their risk for CAD. CAD in India has been reported to present almost a decade earlier than in the West. Deaths occurring due to CAD occur 5–10 years earlier in the Indian subcontinent than in Western countries¹.

We studied the risk factors in a semi-urban area of Tamil Nadu with special reference to the conventional risk factors like diabetes, hypertension, hypercholesterolemia, smoking, and family history of coronary artery disease.

Materials and Methods

The study was a prospective and case controlled study and 50 patients with coronary artery disease and 50 control samples were studied. Institutional ethics committee approval was taken.

Inclusion criteria included a positive treadmill test and/or angiographically proven coronary artery

disease. The control population was taken from patients undergoing master health checkup in our hospital, who did not have any chest pain or proven CAD and were TMT negative.

Data collection- A questionnaire in English and Tamil, was given to all patients diagnosed with coronary artery disease. At the end of the questionnaire, there were 6 questions to be filled by the attending doctor/physician assistant. Interviews were conducted in hospital wards or clinics. Informed consent was obtained from all study subjects.

Blood pressure >140/90mmHg was taken as hypertension. Blood sugar (fasting>110mg/dl, postprandial >140mg/dl after 2 hrs of a meal) were taken as diabetics; Serum cholesterol >200mg/dl was taken as hypercholesterolemia.

Alcohol intake of >4 times a week were taken as alcoholics. This included the Indian whiskey and local beer with an alcohol content of 42.8% and 6-8% respectively. Cigarette smoking of 1 packet/day was taken as smokers, though even smoking 1-4 cigarettes per day showed an increased risk of ischaemic heart disease². Over weight when body mass index (BMI) was >25 kg/m².

Family history of CAD, when a member of the family had proven CAD or there was unexplained sudden death in the family.

30 minutes or more of moderate-intensity physical activity like walking, on most (preferably all) days of the week was taken as evidence of exercise³.

Statistical analysis was done by comparing cases and control subjects using SPSS version 21. The variables in the control and patient group were done using the chi-square test.

Results

Prevalence of CAD increased with increasing age. CAD was found more frequently in men, diabetics and hypertensive's, however this did not reach statistical significance ($p > 0.5$). Hypercholesterolemia, obesity, sedentary lifestyle and alcohol ingestion all proved to be statistically significant risk factors for CAD (Table 1).

Discussion

In our study of 100 patients (50 patients and 50 controls) we found the majority to be males and above 50 years of age. Other studies have shown a greater incidence in young males as well as females^{4,5}. The incidence of diabetes mellitus and hypertension are traditional risk factors and are associated with higher cardio-vascular (CV) risk though in our study it was not statistically significant. Other statistically significant risk factors included smoking, hypercholesterolemia, family history of coronary artery disease, obesity and lack of exercise which was associated with a higher CV risk. This is in concordance with other studies^{6,7,8,9}.

It has been estimated that smoking will be the single largest cause of deaths by 2020. In India, the mortality from tobacco use will rise from 1.4% in 1990 to 13.3% in 2020, a great majority of which, will be due to cardio-vascular diseases^{10,11,12}.

Table 1 - Incidence of CAD with different parameters

Parameters	Cases(no/%)	Controls(no/%)	Odds ratio	P value
Age				
20-29	1(0.04)	5(1)		
30-39	2(0.16)	8(2.5)		
40-49	13(6.76)	21(17.6)		
>50	34(46.2)	21(17.6)		
Sex				
Male	39(55.7)	31(44.3)	2.17	0.08
female	11(36.7)	19(63.3)		
Diabetes				
Yes	27(55.1)	22(44.9)	1.49	0.31
no	23(45.1)	28(54.9)		
Hypertension				
Yes	28(58.3)	20(41.7)	1.90	0.10
no	22(42.3)	30(57.7)		
Dyslipidemia				
Yes	26(68.4)	12(31.5)	3.43	0.002
no	24(38.7)	38(61.2)		
Smoking				
Yes	18(66.7)	9(33.3)	2.56	0.04
no	32(43.8)	41(56.2)		
Family h/o of CAD				
Yes	20(64.5)	11(35.5)	2.36	0.05
no	30(43.5)	39(56.5)		
Obesity				
Yes	34(59.6)	27(62.7)	2.49	0.04
no	16(37.2)	36(61.8)		
Exercise				
Yes	23(38.9)	36(61.8)	0.33	0.01
no	27(65.8)	14(34.1)		
Alcohol				
Yes	22(84.6)	4(15.4)	9.03	0.00
no	28(37.8)	46(62.2)		

p value < 0.05 significant

Hypercholesterolemia is a known factor in the causation of CAD and has been extensively studied in experimental animals and humans. In India, the LDL-C (low density lipoprotein) levels are not very high; there is greater preponderance of the more atherogenic dense LDL particles. The triglyceride levels are high and HDL-C (high density lipoprotein) levels are low. The presence of truncal obesity, metabolic syndrome and diabetes also modulate the impact of dyslipidemia on cardiovascular risk. In literature, this "atherogenic dyslipidemia" is more prevalent and is due to environmental and genetic factors¹⁰. However, that environmental factors play as important a role as genetic factors has been highlighted by a study, where 247 migrants from the Indian sub-continent of Punjabi origin living in West London were compared to 117 of their siblings living in Punjab, India. The study showed that there was a greater body mass index, systolic blood pressure, serum cholesterol, Apo B, lower HDL-C and higher fasting blood glucose in the West London cohort (p value <0.01)¹³.

Lipid profile includes triglyceride (TG), total cholesterol (TC), HDL-C (high density lipoproteins) and LDL-C (low density lipoproteins). The TC, TG, and HDL-C are measured directly using enzymatic assays and LDL-C is derived indirectly. As consumption of food affects TG levels directly a fasting sample is essential to estimate LDL-C accurately. Absence of proximity to laboratories performing these tests in rural and semi-urban areas, may make testing in fasting state impractical for the patient. Thus, the Indian population maybe showing a spurious hypertriglyceridemia, if testing is not done in the fasting state. This can be overcome by calculating non-HDL-C which is a good alternative and is obtained by subtracting HDL-C from TC. It has the additional advantage of measuring atherogenic lipid molecules like VLDL (very low density lipoproteins), IDL (intermediate density lipoproteins), chylomicrons, chylomicron remnants and lipoprotein a¹⁴.

Family history of CAD was an important risk factor in young Indian patients as was seen in our study. Modifiable variables like blood pressure, ApoB/ApoA1 ratio, serum cholesterol, and abdominal obesity are partly under genetic control. Potential genetic factors such as variance of genes involved in vascular homeostasis, hemostatic factors, lipid metabolism, and other metabolic factors may contribute to CAD¹⁵. In a large, prospective study, Parmar reported that 15% of coronary events were because of family history of coronary artery disease, at any age (not premature coronary artery disease) in first-degree relatives¹⁶.

Obesity has been attributed to heart disease by increasing blood pressure, blood glucose and lipids^{6,15}. Physical inactivity is an important risk factor for the development of CAD, hypertension, type II diabetes mellitus, obesity and, dyslipidemia. Physical activity has been shown to reduce TG and reduce the LDL-C particle size thus directly improving "atherogenic dyslipidemia"^{17,18,19}.

Our study showed a strong correlation of CAD with alcoholism. This is probably of semi-urban population

alcohol consumption is usually associated with smoking, dietary indiscretion and lack of exercise. Therefore, alcoholism in this sub-group maybe taken a surrogate for coronary risk. Consumption of alcohol > 100g/day is a risk factor atherogenesis and consumption of <50g/day is protective due to the antithrombotic and inhibition of the atherogenic action of high levels of LDL²¹.

Limitations of the study

Though there was a trend in traditional risk factors as causative for CAD, the number of study patients were insufficient to bring out statistical significance. Also, since the study was conducted in a semi-urban area the levels of stress was less compared to the urban counterpart; stress is known to contribute to the pathogenesis of both diabetes and hypertension. Insulin resistance, levels of lipoproteins, plasma fibrinogen, plasminogen activator inhibitor-1, markers of infection or inflammation, raised homocysteine levels, which have been associated with atherosclerosis could not be assessed and will be evaluated in further studies²².

Conclusion

Our study does bring out the significance of hypercholesterolemia, family history of CAD, obesity and lack of exercise in the aetiopathogenesis of CAD.

Authors declare no conflict of interest.

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Original Article

Prevalence of Glucose Tolerance Test abnormalities in South Indian Sub-fertile PCOS women

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Abstract

Objective: To study the prevalence of Glucose Tolerance Test abnormalities in PCOS women attending the infertility clinic in a tertiary care hospital.

Methods: 149 PCOS women who attended the infertility clinic between September 2007 –August 2009, were subjected to Oral Glucose Tolerance Test (GTT) with 75 grams glucose load after ruling out other causes of anovulation. Blood sugar values were categorized as normal, impaired or Type 2 Diabetes Mellitus by WHO 1999 criteria.

Results: 149 women were enrolled in the study, 125 women (83.8%) had normal GTT; Impaired GTT was seen in 21 women 21/149 (14.09%), 3 women were Type 2 DM with the prevalence of 2.017% (03/149). There was no difference between the two groups in terms of age, BMI, family history of DM, cycle irregularity, hyper androgenic features such as acne or hirsutism.

Conclusion: The prevalence of abnormal GTT in the population studied was 17%. As there are no specific indicators to differentiate the women at risk of abnormal glycaemic status, it is wiser not to limit screening to any subset population of PCOS.

Key Words: PCOS, GTT abnormalities, metabolic syndrome

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Introduction

Polycystic ovarian syndrome (PCOS) is the commonest cause of anovulation and subfertility¹. Women with PCOS have higher risk of metabolic syndrome and metabolic derangements like diabetes in the long term². As most women present to a fertility specialist in their reproductive years, it is important to know the prevalence of pre diabetes and diabetes in this population to direct counseling at changing life styles which helps in decreasing the severity or delaying the onset of diabetes mellitus and cardiovascular complications³. WHO in 2008 estimated the prevalence of elevated fasting glucose /those on treatment to be between 10-12.4% in Indian population⁴.

Methodology

Aim : To estimate the prevalence of GTT abnormalities in PCOS women attending the fertility clinic.

Study design: Retrospective cohort study.

Setting: Reproductive medicine unit outpatient clinic in a tertiary care teaching hospital.

Study population: Women attending the outpatient department for fertility concern.

Inclusion criteria: Women diagnosed as PCOS according to Rotterdam criteria⁵. Rotterdam criteria being 1. oligo/anovulation 2. clinical or biochemical hyper androgenism (clinical hyper androgenism defined by

Ferriman Gallway scoring system and a score of more than 6-8 is considered as clinical hyper androgenism) 3. Ultrasound features of polycystic pattern in one or both ovaries. (polycystic pattern is defined as more than 12 follicles of less than 10 mm diameter and ovarian volume of $\geq 10\text{cm}^3$)⁵.

Exclusion criteria

Women with other causes of anovulation like

1. Thyroid, prolactin abnormalities
2. Premature ovarian failure.

Others

3. Women diagnosed to be a diabetic.
4. Women on metformin.

Women were categorized as PCOS based on Rotterdam Criteria. Thyroid and prolactin levels were done to rule out other causes of oligo/anovulation. Women eligible for the study were subjected to a 75 grams glucose challenge with overnight fasting. Sampling of venous blood and urine were done at fasting state and 60 minutes and 120 minutes of glucose challenge. Dipstick method was used to assess glycosuria and Hexokinase method for venous plasma glucose estimation.

Women were categorized as euglycaemic, impaired GTT or Diabetes mellitus according to WHO criteria (1999)^{4&6} (Table 1).

Table 1-Reference Range: WHO 1999 (Venous plasma)

Classification	Fasting values	2hrs
Normal	<6mmol/L (80 - 110 mg/dL)	<7.8mmol/L (<140mg/dL)
Diabetes mellitus	>7mmol/L and/or (>126 mg/dL))	>11 mmol/L (≥ 200 mg/dL)
Impaired GTT	>6.1 mmol <7 mmol/L (111–125 mg/dL)	7.8-11mmol/L (140 - 200 mg/dL)

Statistical analysis

Descriptive analysis of explanatory variables like age, menstrual cycle, body mass index, family history, acne, hirsutism and hypothyroidism and outcome parameters were done. The statistical significance of the differences and 95% CI were assessed by using χ^2 test, Mann Whitney U test and Kruskal Wallis Test as appropriate. IBM SPSS statistics, version 21 was used for the analysis⁷.

Results

Two year case records and reports between the period September 2007 - August 2009 were searched and relevant data were entered and analyzed. One hundred and forty nine women were eligible for data analysis. 63.09% of women were less than 30 years of age (Table -2), 47.30% were in normal Body Mass Index group (Table-3). Family history of diabetes was present in 42.28% of population studied, 65.10% had minimal hirsutism and 16.78% had associated hypothyroidism.

Table 2: Age distribution

Age	Count	%
20-25	23	15.44
25-30	71	47.65
30-35	42	28.19
35-40	13	8.72

Table 3 : BMI distribution

BMI	Count	%
18-25	70	47.30
26-29	43	29.05
30-35	31	20.95
> 35	4	2.70

125 women (83.8%) had normal GTT, impaired GTT was seen in 14.09% of women (21/149), whereas 2.01% of the study population (3/149) had Type 2 Diabetes. (Table-4)

Table 4 : GTT results in the study group

GTT	No.	%
Normal	125	83.89
Impaired GTT	21	14.09
Type 2 DM	3	2.01

Most of the women with impaired GTT (85.61%) were in the age group more than 25 yrs, but nearly half of them (42.86%) were of normal BMI. Whereas, all the type 2 DM were in overweight or obese category. Family history of diabetes was present only in 38.1% of women with impaired GTT and 33.33% of type 2 DM. There was no significant difference in distribution of variables viz. age, BMI, presence of family history of DM, features of clinical hyperandrogenism between women with normal GTT and those with impaired GTT (Table-5).

Descriptive analysis of the variables affecting outcome did not show any difference between the three categories.

Discussion

Impaired glucose tolerance and diabetes increases the long term morbidity and it indirectly influences the expenditure on health, loss of working hours and the money spent on health care by the state. Early diagnosis and defining risk factors are essential. As the prevalence is likely to vary between people of different ethnicity, it is vital to assess the prevalence in each population.

The impaired GTT was seen in 14.09% and type 2 DM in 2.01% in our population. This concurs with a study on PCOS subjects of similar ethnicity done in Tamil Nadu⁸. In this the reported incidence of impaired GTT was 11.7% and DM was seen in 5.8%. The above mentioned study defined age more than 25 yrs and central obesity as high risk factors for metabolic syndrome. Our study did not show any significant difference between the groups with GTT abnormalities and normal GTT, considering age and BMI distribution, presence of family history of type 2 DM and presence or absence of clinical hyper androgenism.

GTT is considered invasive, time consuming and causes inconvenience to patients compared to the estimation of fasting, post prandial blood glucose and HbA1C assessment. This issue was addressed by a prospective controlled study done on 252 Turkish PCOS women⁹ where GTT was found to be a better method to assess Glucose intolerance compared to HbA1C as the HbA1C cut off of 5.6% missed the glucose intolerance in 50% of the PCOS subjects. It is important to note that the prevalence showed was similar. The study population had IGT in 14.3% and Type 2 DM in 2%. Contrary to our data age, BMI were significantly higher in PCOS women with GTT impairment.

Though the South Asian population is considered to have increased preponderance to impaired glucose metabolism (ESHRE/ASRM¹⁰) here the prevalence in our population was much lower than the American study. In the American study by Legro et al¹¹ on different American ethnic population, the prevalence of IGT was 31.1% of IGT and 7.5% of DM. This is high compared to our group. But the mean BMI of 29.9±8.1 to 35.9±8 was much higher in the American group.

The obvious limitation of our study was the small sample size.

Table 5 : Analysis of variables

		GTT						Kruskal Wallis	
		Normal		Impaired		Type 2-Diabetes		Test	
		Count	%	Count	%	Count	%	Chi-Square Value	Sig.
Age	20-25	19	15.20	3	14.29	1	33.33	4.419	.110
	25-30	63	50.40	6	28.57	2	66.67		
	30-35	33	26.40	9	42.86	0	.00		
	35-40	10	8.00	3	14.29	0	.00		
BMI	18-24	61	49.19	9	42.86	0	.00	3.667	.160
	25-29	35	28.23	7	33.33	1	33.33		
	30-35	25	20.16	4	19.05	2	66.67		
	> 35	3	2.42	1	4.76	0	.00		
Menstrual Cycle	Regular	59	47.20	8	38.10	0	.00	3.083	.214
	Irregular	66	52.80	13	61.90	3	100.00		
Family history	Yes	54	43.20	8	38.10	1	33.33	.290	.865
	No	71	56.80	13	61.90	2	66.67		
Acne	Yes	12	9.60	0	.00	1	33.33	4.379	.112
	No	113	90.40	21	100.00	2	66.67		
Hirsutism	Yes	80	64.00	14	66.67	3	100.00	1.686	.430
	No	45	36.00	7	33.33	0	.00		
Galactorrhea	No	119	95.20	20	95.24	3	100.00	.150	.928
	Yes	6	4.80	1	4.76	0	.00		
Hypothyroid	Yes	17	13.60	6	28.57	2	66.67	8.287	.016
	No	108	86.40	15	71.43	1	33.33		

Conclusion

PCOS is known to be associated with metabolic derangements which have far reaching consequences in life. Our study revealed a prevalence of GTT abnormality of 16% in PCOS women of reproductive age group. Though the prevalence is less compared to the other studies done in Sri Lanka, Asia and America¹²⁻¹⁵, considering the population in India, our absolute number of women with impaired glucose tolerance and type2 DM is expected to be high. As there are no variables in our study to restrict screening to particular group of PCOS women, it is recommended that every PCOS women be offered GTT to rule out abnormal glucose metabolism in them.

Acknowledgement

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Authors declare no conflict of interest.

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Carb Is Better, When Eaten Later!

Obese individuals with type 2 diabetes should maintain their blood sugar levels as close to normal as possible, after a meal, in order to forestall the development of complications. This is definitely dependent on what they eat. But what is not clear is whether it is also related to the order in which the various nutrients are consumed. In a new study reported in *Diabetes Care*, the researchers have tried to answer this. The study was carried out on obese diabetics of both sexes. It was found that when the participants ate vegetables and proteins before eating carbohydrates, their blood sugar levels were about 29 percent lower 30 minutes after starting the meal than when they ate carbohydrates first. The same pattern was noted after 60 and 120 minutes. Apparently, vegetables and proteins render carbohydrates less glycemic by delaying their absorption. The study suggests that diabetics need not completely avoid carbohydrates; but they have to remember to eat it after the salads and proteins (<http://care.diabetesjournals.org/content/38/7/e98.full>)

- Dr. K. Ramesh Rao

Original Article

A New Simple Test for Checking Vitality of Spermatozoa

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Abstract

Objective: Hypo-osmotic swelling (HOS) test was done to assess the vitality of spermatozoa. Sterile water is easily available and inexpensive when compared to HOS reagent. Efficacy of sterile water is checked in comparison with Hypo-osmotic swelling (HOS) Reagent for assessing the vitality of human spermatozoa.

Setting: Prospective study conducted at a tertiary referral centre and Research Institute.

Patient Criteria: Study includes 30 patients who had come for routine semen analysis. Consent forms had been taken from the patients.

Methodology: All samples were included except azoospermic samples. Semen sample was subjected to HOS test, sterile water test, Eosin - Nigrosin test (EN) after routine semen analysis.

Results: Average number of vital spermatozoa of HOS test, sterile water test and EN test are 55.83%, 58.10% and 59% respectively. Average number of vital spermatozoa of HOS test were compared with sterile water test ($p=0.468$), average number of vital spermatozoa of HOS test were compared with EN test ($p=0.286$) and average number of vital spermatozoa of sterile water test were compared with EN test ($p=0.847$). The p -value for all the three tests together (HOS test, sterile water test, Eosin nigrosin test (EN)) showed 0.567 which is statistically insignificant thereby indicating that there was no major difference between the three tests.

Conclusion: Sterile water can replace HOS reagent for vitality test of spermatozoa. It might prove beneficial to the patient as it is less expensive and cost-effective.

Key Words: Human spermatozoa, HOS test, Vitality, Sterile water

Chettinad Health City Medical Journal 2015; 4(1): 24 - 27

Introduction

Vitality is defined as presence of structural and functional intact membrane of the cell. Hypo-osmotic swelling test (HOS test) is a vitality test done for spermatozoa. It is an additional sperm function test, normally used to identify the percentage of vital spermatozoa within semen groups for asthenozoospermia, Immotile Cilia syndrome, occasionally motile spermatozoa and spermatozoa retrieved from testicular biopsies, where the motility of the spermatozoa is diminished. A simple new test using sterile water can be used to assess the vitality thereby making it simpler and much more cost effective.

HOS test was developed by Jeyendran et al, in 1984¹. The basic HOS reagent is 150 mOsm. It contains 0.735g of sodium citrate dihydrate and 1.351g of D-fructose in 100ml of purified water¹. The basic principle of HOS test is that solution enters the spermatozoa under hypo-osmotic conditions due to osmosis. The sperm tail then expands and coils depending on the sperm membrane function and integrity. Sperm tail does not coil if the sperm membrane is damaged. Sterile water test works on the same basic principle as HOS test. Sterile water is 0 mOsm which is hypo-osmotic. The principle of Eosin Nigrosin test is that

spermatozoa with intact membrane integrity do not take up the stain and therefore are colourless. Spermatozoa in which membrane integrity has been lost take up the stain, therefore they are pink in colour². The aim of our study was to check whether sterile water can be used to assess the vitality of spermatozoa.

Methodology

Patient criteria: Prospective study was done at Chettinad Hospital & Research Institute. All types of semen samples were included except azoospermic samples. HOS reagent, sterile water and eosin nigrosin reagent were used for this study. Samples were subjected to HOS test, sterile water test and eosin nigrosin test after the initial semen analysis had been done according to WHO manual 2010. All the semen samples which were about to be discarded after initial semen analysis were used for this study. Thirty samples were included in the study.

HOS test: HOS reagent which was used belongs to Cell Life Company, Vishakhapatnam. Protocol was followed as per instructions given in the HOS test kit.

- 1 ml of HOS reagent (150 mOsm/L) was incubated for normozoospermic samples in an incubator at

37°C for 20 minutes. 0.5 ml of HOS reagent was incubated for oligozoospermic samples in an incubator at 37°C for 20 minutes.

2. One drop (5 µl) of semen was mixed with HOS reagent and incubated for 10 minutes.
3. One drop (5 µl) of well mixed semen was taken on the glass slide and a cover slip was placed on it. Hundred spermatozoa were counted randomly. Spermatozoa with coiled tails were considered as vital and uncoiled tails were considered as dead (figure 1).

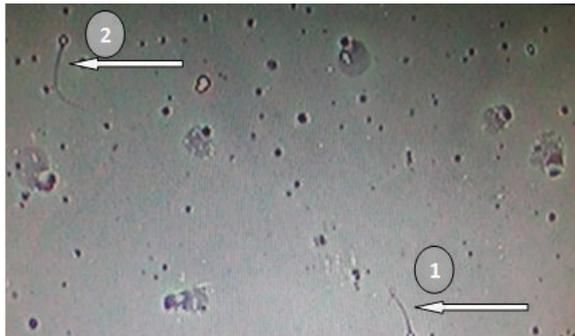


Fig 1 - (1) Coiled tail- vital. (2). Straight tail- Non vital

Sterile Water Test Protocol

1. 1 ml of sterile water (0 mOsm/L) was incubated for normozoospermic samples in an incubator at 37°C for 20 minutes. 0.5 ml of sterile water was incubated for oligozoospermic samples in an incubator at 37°C for 20 minutes.
2. One drop (5 µl) of semen was mixed with sterile water and incubated for 10 minutes.
3. One drop (5 µl) of well mixed semen was taken on the glass slide and a cover slip was placed on it. Hundred spermatozoa were counted randomly. Spermatozoa with coiled tails were considered as vital and uncoiled tails were considered as dead (figure 2).



Fig 2 - (1) Coiled tails. (2). Straight tail- Non vital

Eosin Nigrosin Test Protocol

Eosin nigrosin kit which was used belongs to Cell Life Company, Vishakapatnam. Protocol was followed as per instructions given in the Eosin nigrosin kit.

1. One drop (5 µl) of eosin nigrosin stain was mixed with one drop (5 µl) of semen in an eppendorf tube and kept for 25 seconds.
2. A drop (5 µl) of well mixed sample was taken from the eppendorf tube and placed on the glass slide and thin smear was made on the glass slide. Slide was incubated at 37°C in an incubator for 10 minutes. Hundred spermatozoa were examined. Pink coloured heads of spermatozoa were considered as non-vital and colorless heads were considered as vital.

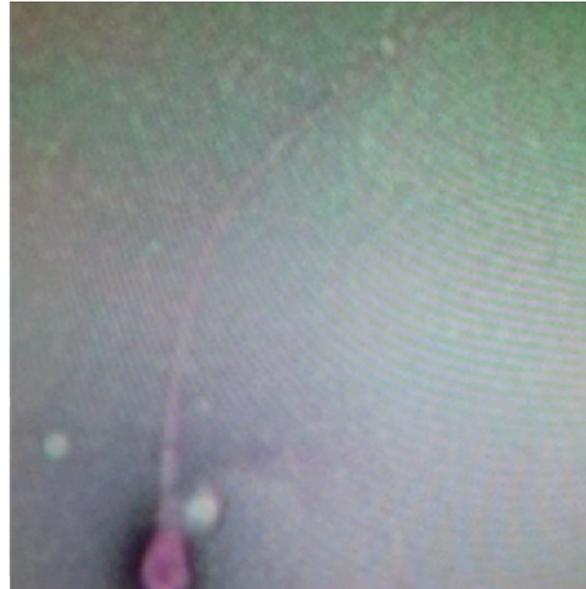


Fig 3 - Pink Coloured Head - Nonvital



Fig 4 - Colourless Head - Vital

Statistical Analysis

Statistical analysis was done with Mann-Whitney U test and Kruskal-Wallis H test. Both the tests were done by comparing the mean of the variables of HOS test, Sterile water test and Eosin-nigrosin test.

Results

Thirty samples were included in the study. Mean age of the patients was 33.6 years. Mean spermatozoa concentration was 78.16 million per ml. Mean total motility of spermatozoa was 58.8% (table 1).

Patient's criteria (n= 30)	Mean
Age(years)	33.6
Concentration(million /ml)	78.16
Motility (%)	58.8

Table 1 - Mean criteria of patients

VARIABLES	MIN	MAX	MEAN	SD	Mean difference		P VALUE
					MEAN	SD	
HOST (%)	30	89	55.83	14.66	2.27	0.48	0.468
Water (%)	30	80	58.10	14.18			
HOST (%)	30	89	55.83	14.66	3.17	0.34	0.286
EN (%)	30	80	59.00	14.32			
Water (%)	30	80	58.10	14.18	0.90	0.14	0.847
EN (%)	30	80	59.00	14.32			

Table 2 - Comparison between mean of the variables of vital spermatozoa of HOS Test, Sterile Water Test, Eosin – Nigrosin Test(En)

Statistical Analysis: Mann-Whitney U test. Statistically significant if P<0.05

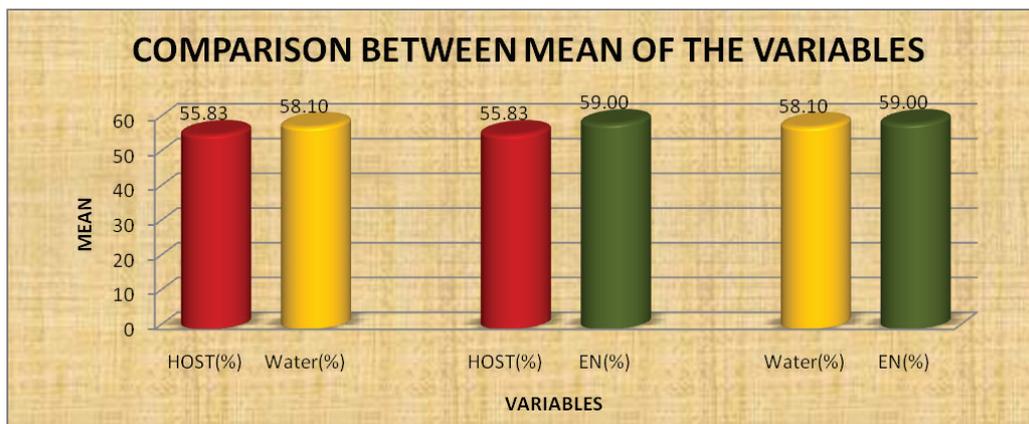


Fig 5 - Histograms representing comparison between any two tests . HOS test – Red, Sterile water test – Yellow and eosin nigrosin test – Green.

VARIABLES	MIN	MAX	MEAN	SD	P VALUE
HOST (%)	30	89	55.83	14.66	0.567
Water (%)	30	80	58.10	14.18	
EN (%)	30	80	59.00	14.32	

Table 3 - Comparison between mean of the variables of vital spermatozoa of HOS test, sterile water test, eosin – nigrosin(en) test

Statistical Analysis: Kruskal-Wallis H test. Statistically significant if P<0.05

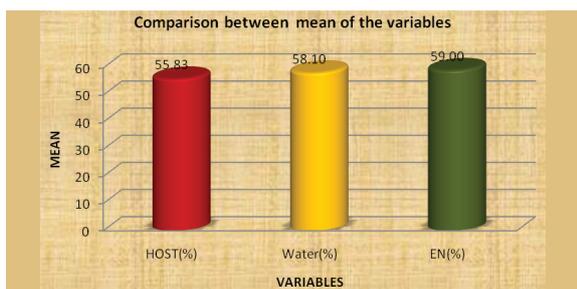


Fig 6 - Histograms representing comparison of all the three tests. HOS test – red, sterile water test – yellow and eosin nigrosin test – green.

Discussion

Sterile water test (0 mOsm), HOS test (150 mOsm) and Eosin nigrosin tests were compared to check the vitality of spermatozoa. All the three tests gave similar results. The vital spermatozoa of the three tests have showed correlation with total motility of spermatozoa. Eosin nigrosin test checks the membrane integrity of the spermatozoa but they cannot be used for Intracytoplasmic Sperm Injection (ICSI) once stained. However, Spermatozoa assessed through HOS test can be used for ICSI⁴. Similar study comparing HOS test and sterile water test was done on Drone spermatozoa³. There was no difference in results of HOS test and sterile

water test in Drone spermatozoa³. Aneuploidy rates are similar in morphologically normal vital immotile spermatozoa selected through HOS test and normal motile spermatozoa⁵.

Conclusion

The degree of hypo-osmolarity of sterile water (omOsm) to spermatozoa is more when compared to HOS reagent(150 mOsm). Coiling of tail takes place faster when compared to HOS test. Sterile water is less time consuming and cost effective. Therefore sterile water can be used as alternative to HOS reagent.

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Authors declare no conflict of interest.

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Maternal Diabetes and Offspring's Intelligence

According to a new study from Denmark, pregnant women with type I diabetes should keep the blood glucose level under control; otherwise, the offspring's cognitive development may be adversely affected. In that study, which is published in the latest edition of *Diabetes Care*, academic performance of 707 primary school children of mothers with type I diabetes, was correlated with blood glucose levels of their mothers during and before pregnancy and also with academic performance of 60000 children of non-diabetic mothers. It was found that children of mothers with good control of blood sugar performed better than average academically when compared to their peers in general population. Women with the best diabetes control in pregnancy had offspring that performed better academically than offspring of women without diabetes! Conversely, children of mothers with poorly controlled diabetes had lower grades. This correlation was found to be independent of parental education. As no such studies have been conducted with other types of diabetes, the results cannot be extrapolated.

- Dr. K. Ramesh Rao

Original Article

Students Perception About the Educational Environment

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Abstract

Background: The educational environment is fundamental to effective student learning. It has been shown to significantly impact their attitudes and professional progress and is critical for personal and social well-being. The present survey was conducted among the dental students and interns of Chettinad Dental College and Research Institute to assess their perception about the educational environment in the institution.

Materials and Methods: A cross-sectional questionnaire survey employing convenience sampling was conducted among dental students and interns of Chettinad Dental College. The survey instrument used was Dundee Ready Education Environment Measure (DREEM). Collected forms filled with responses were entered in Microsoft Excel – 2010 and then subjected to statistical analysis using SPSS (Version 17).

Results: 262 students participated in the present study. Of the 50 items of DREEM inventory, 13 items were scored more than 3.0, 34 items were scored between 2.0 and 3.0 and 3 items were scored less than 2.0, Overall DREEM score among the dental students and interns is 136.09 ± 17.39 and there is a difference in mean DREEM score across years of study ($p < 0.05$) and no difference across gender in overall DREEM score ($p > 0.05$).

Conclusion: Chettinad Dental College and Research Institute had overall a positive environment; though the negative areas in the institution are minimal, there still exists large areas which require lots of improvement in all the subscales of DREEM.

Key Words: DREEM, Dental Students, Educational Environment

Chettinad Health City Medical Journal 2015; 4(1): 28 - 31

Introduction

The educational environment is fundamental to effective student learning. It has been shown to significantly impact their attitudes and professional progress and is critical for personal and social well-being¹. A number of factors ranging from class size, leisure time, teaching methodologies and assessment procedures to relations with peers and faculty, ethical climate and extracurricular opportunities, may significantly influence student's perceptions and experiences².

Dental educators need to be sensitive and responsive to the concerns of dental students. It is the responsibility of all dental institutions to ensure that future dentists are being nurtured in a supportive and challenging environment that promotes learning in a positive way^{3,4}. Thus effective management of learning is aided by understanding the educational environment and introducing appropriate changes. The Dundee Ready Education Environment Measure (DREEM)⁵ is specific to the unique environment experienced by students in medical and healthcare related courses⁶. In India, there are 301 dental colleges and in the state of Tamil Nadu there are 29 dental colleges, Chettinad Dental College and Research Institute is one among them⁷ established in the year 2007, the college has an annual intake of 100 undergraduate dental students. It is essential to analyse

the student's and intern's perception regarding their educational environment, as it provides vital information for personal and institutional development. Hence the present survey was conducted among the dental students and interns of Chettinad Dental College and Research Institute to assess their perception about the educational environment in the institution.

Materials and Methods

A cross sectional descriptive study, employing convenience sampling method was conducted to assess their perception about the educational environment among the students and interns of Chettinad Dental College and Research Institute, Kelambakkam. The survey instrument used was Dundee Ready Education Environment Measure (DREEM)⁵ consists of 50 items answered on 5-point likert scale which are scored from 0 (strongly disagree) to 4 (strongly agree). Items with a mean score of 3 and above are considered positive and items with a mean score of 2 and below are considered as problem areas and items with a mean score between 2 and 3 are considered as aspects of the educational environment that require enhancement. DREEM has five subscales, the subscales are as follows:

- Students' perception of Learning (SPL) – 12 items with maximum score of 48

- Students' perception of Teachers (SPT) – 11 items with a maximum score of 44
- Students' Academic self-perception (SASP) – 8 items with a maximum score of 32
- Students' perception of Atmosphere (SPA) – 12 items with a maximum score of 48
- Students' Social self-perception (SSSP) – 7 items with maximum score of 28.

Prior to the start of the study approval was obtained from the college authorities and explanation was given to all the dental students and interns regarding the study and informed consent was obtained from the students who were willing to participate in the study, Students who were not willing to participate in the study were excluded.

Self – administered questionnaires were distributed to the students during the end of their academic year. Data collection was done for a period of 15 days, from 16th June 2014 to 30th June 2014 and the students were asked to go through the statements carefully and asked to 'tick' the appropriate answer of their choice. The filled questionnaires were collected by placing a collection box in the Department of Public Health Dentistry during the aforementioned time period.

Collected forms filled with responses were entered in Microsoft Excel – 2010 and then subjected to statistical analysis using SPSS (Version 17).

Frequency tables were computed and independent samples t-test and One way ANOVA is used for the

comparison of mean domain scores and DREEM score across gender and between year of study among dental students.

Results

A total of 395 students and interns were in the academic year 2013-14, among them 262 students and interns (response rate – 67%) participated in the present study. Fig 1 depicts the distribution of study subjects according to year of study and gender. Table 1 depicts the comparison of mean DREEM score across years of study, the following domains. Students perception of Learning (SPL), Students perception of Teachers (SPT), Students perception of Atmosphere (SPA) and Students Social self-perception (SSSP) of DREEM showed a significant difference across year of study and there has been a significant decrease in the overall DREEM score across year of study with first year students having the highest DREEM score (140.30 ± 16.69), second year students (138.79 ± 14.65), third year students (135.55 ± 14.74), final year students (135.09 ± 13.15) and interns (128.89 ± 27.40) having the lowest DREEM score.

Table 2 depicts the mean DREEM global and subscale score among the dental students and interns, for students perception of learning (SPL) 8 out of 12 items scored between 2.0 and 3.0, and 4 items scored more than 3.0 and the overall mean score for this domain was (34.35 ± 5.33) and there was no difference across gender.

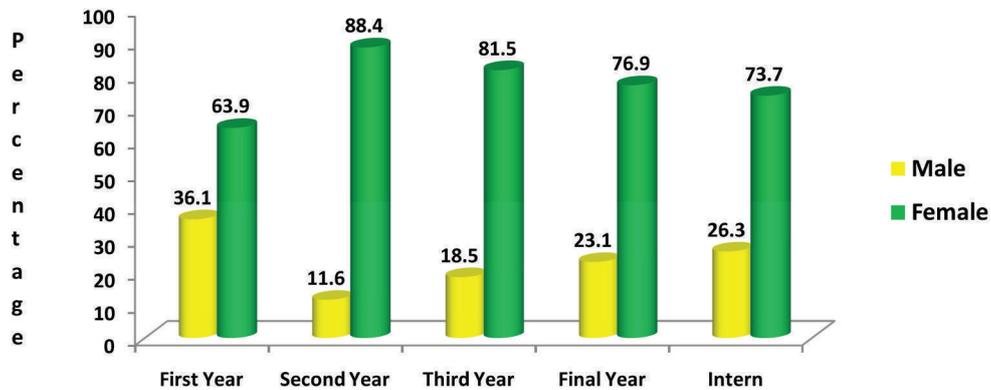


Fig 1: Depicts the distribution of study subjects according to year of study and gender

Domain	First Year*	Second Year*	Third Year*	Final Year*	Intern*	f	df	p-value
Students perception of Learning*	35.31 ± 5.22	34.95 ± 4.95	33.85 ± 5.00	34.60 ± 4.20	32.53 ± 7.51	1.951	271	0.102
Students perception of teachers*	29.54 ± 4.29	28.60 ± 2.92	30.08 ± 2.74	30.62 ± 2.35	28.18 ± 6.16	3.62		0.007
Students' academic self-perception*	22.90 ± 3.97	23.09 ± 4.63	22.63 ± 4.17	22.38 ± 3.30	21.11 ± 5.34	1.426		0.225
Students perceptions of atmosphere*	33.15 ± 5.54	33.09 ± 4.50	31.57 ± 4.50	29.66 ± 4.45	29.08 ± 7.63	6.145		0.000
Students social self-perceptions*	19.39 ± 3.09	19.05 ± 2.49	17.43 ± 2.94	17.83 ± 3.04	18.00 ± 4.17	4.156		0.003
Total DREEM score*	140.30 ± 16.69	138.79 ± 14.65	135.55 ± 14.74	135.09 ± 13.15	128.89 ± 27.40	2.927		0.021

Table 1: Comparison of mean DREEM score and domain scores across years of study

*One way ANOVA, (p<0.05 – Statistically Significant)

In the domain on Students' perception of teachers (SPT) out of 11 items 5 were scored more than 3, 4 items were scored between 2.0 and 3.0 and 2 items were scored less than 2.0. The items, 'The teachers ridicule the students' and 'The students irritate the teachers' with negative score are scored less than two, comparison of mean scores across gender in this domain had showed a significant difference in score. For the following items 'The teachers are authoritarian' and 'The students irritate the teachers' ($p < 0.05$), the mean score domain was (29.59 ± 3.79).

In the domain of Students' academic self-perception (SASP) among the 8 items, 7 items were scored

between 2.0 and 3.0 and 1 item is scored above 3.0, there was no gender difference in individual item score and overall score for this domain, the mean overall score for this domain was (22.49 ± 4.21).

In the domain of Students' perception of atmosphere (SPA) among the 12 items, 9 items were scored between 2.0 and 3.0, 2 items were scored above 3.0 and 1 item 'I find the experience disappointing' (1.89 ± 1.01) was scored less than 2, there was a significant difference across gender in response to the following item, 'I am able to concentrate well' ($p < 0.05$) and the mean overall score for this domain was (31.36 ± 5.47).

Table 2: Mean DREEM global and subscale score among the dental students and interns

Q. No.	Question	Total (Mean \pm SD)	Male* (Mean \pm SD)	Female* (Mean \pm SD)	t-value	p-value
	Students Perception Of Learning	34.35 \pm 5.33	34.62 \pm 4.54	34.26 \pm 5.56	0.479	0.633
1	I am encouraged to participate in class	3.03 \pm 0.78	2.98 \pm 0.72	3.04 \pm 0.81	0.479	0.633
7	The teaching is often stimulating	2.89 \pm 0.88	2.98 \pm 0.76	2.87 \pm 0.90	0.95	0.343
13	The teaching is student-centered	2.88 \pm 0.84	2.91 \pm 0.76	2.88 \pm 0.88	0.259	0.796
16	The teaching is sufficiently concerned to develop my competence	2.98 \pm 0.85	3.00 \pm 0.81	2.97 \pm 0.86	0.237	0.813
20	The teaching is well focused	3.16 \pm 0.77	3.30 \pm 0.60	3.12 \pm 0.80	1.657	0.099
22	The teaching is sufficiently concerned to develop my confidence*	3.02 \pm 0.83	3.05 \pm 0.82	3.01 \pm 0.84	0.31	0.757
24	The teaching time is put to good use	3.10 \pm 0.77	3.08 \pm 0.86	3.11 \pm 0.74	0.294	0.769
25	The teaching over- emphasized factual learning*	2.65 \pm 0.82	2.67 \pm 0.92	2.65 \pm 0.79	0.194	0.846
38	I am clear about the learning objectives of the course	2.90 \pm 0.89	2.81 \pm 0.95	2.93 \pm 0.87	0.215	0.347
44	The teaching encourages me to be an active learner	2.93 \pm 0.83	2.84 \pm 0.89	2.96 \pm 0.82	0.107	0.327
47	Long term learning is emphasized over the short term	2.72 \pm 0.87	2.83 \pm 0.91	2.68 \pm 0.86	0.978	0.245
48	The teaching is too teacher-centred*	2.08 \pm 1.01	2.17 \pm 1.07	2.05 \pm 1.00	0.284	0.396
	Students' perception of teachers	29.59 \pm 3.79	30.03 \pm 3.49	29.45 \pm 3.88	1.068	0.286
2	The teachers are knowledgeable	3.53 \pm 0.61	3.52 \pm 0.59	3.53 \pm 0.621	0.205	0.837
6	The teachers are patient with patients	3.16 \pm 0.80	3.06 \pm 0.87	3.19 \pm 0.78	1.131	0.259
8	The teachers ridicule the students*	1.74 \pm 1.11	1.92 \pm 1.17	1.68 \pm 1.09	1.53	0.127
9	The teachers are authoritarian*	2.43 \pm 0.96	2.69 \pm 0.90	2.35 \pm 0.97	2.451	0.015*
18	The teachers have good communication skills with patients	3.11 \pm 0.83	3.22 \pm 0.78	3.08 \pm 0.84	1.19	0.235
29	The teachers are good at providing feedback to students	2.83 \pm 0.82	2.72 \pm 0.89	2.87 \pm 0.80	1.28	0.201
32	The teachers provide constructive criticism here	2.47 \pm 0.95	2.53 \pm 0.85	2.45 \pm 0.98	0.615	0.539
37	The teachers give clear examples	3.03 \pm 0.79	2.98 \pm 0.78	3.05 \pm 0.80	0.558	0.578
39	The teachers get angry in class*	2.13 \pm 1.08	2.14 \pm 1.02	2.13 \pm 1.10	0.07	0.944
40	The teachers are well prepared for their classes	3.17 \pm 0.85	2.98 \pm 0.86	3.22 \pm 0.85	1.94	0.053
50	The students irritate the teachers*	1.99 \pm 1.14	2.27 \pm 1.12	1.90 \pm 1.14	2.221	0.027*
	Students' academic self-perception	22.49 \pm 4.21	22.22 \pm 3.75	22.58 \pm 4.35	0.593	0.553
5	Learning strategies which worked for me before continue to work for me now	2.46 \pm 1.01	2.28 \pm 0.98	2.51 \pm 1.07	1.617	0.107
10	I am confident about passing this year	3.24 \pm 0.85	3.22 \pm 0.76	3.25 \pm 0.88	0.216	0.829
21	I feel I am being well prepared for my profession	2.99 \pm 0.88	3.03 \pm 0.85	2.97 \pm 0.89	0.475	0.635
26	Last year's work has been a good preparation for this year's work	2.90 \pm 0.82	2.77 \pm 0.85	2.95 \pm 0.81	1.538	0.125
27	I am able to memorize all I need *	2.34 \pm 0.98	2.33 \pm 1.00	2.34 \pm 0.98	0.093	0.926
31	I have learned a lot about empathy in my profession	2.83 \pm 0.80	2.89 \pm 0.85	2.81 \pm 0.78	0.72	0.471
41	My problem-solving skills are being well developed here	2.76 \pm 0.87	2.77 \pm 0.88	2.76 \pm 0.87	0.048	0.962
45	Much of what I have to learn seems relevant to a career in medicine	2.98 \pm 0.80	2.94 \pm 0.81	2.99 \pm 0.80	0.459	0.647
	Students' perception of atmosphere	31.36 \pm 5.47	30.91 \pm 5.39	31.50 \pm 5.50	0.758	0.449
11	The atmosphere is relaxed during the ward teaching	2.35 \pm 1.03	2.45 \pm 1.15	2.32 \pm 1.00	0.882	0.378
12	This school is well timetabled	3.01 \pm 0.93	3.05 \pm 0.98	3.00 \pm 0.92	0.35	0.727
17	Cheating is a problem in this school *	2.19 \pm 1.22	2.23 \pm 1.17	2.18 \pm 1.23	0.323	0.747
23	The atmosphere is relaxed during lectures	3.05 \pm 0.90	3.03 \pm 0.81	3.05 \pm 0.93	0.167	0.868
30	There are opportunities for me to develop interpersonal skills	2.81 \pm 0.94	2.72 \pm 0.95	2.84 \pm 0.94	0.86	0.386
33	I feel comfortable in the class socially	2.99 \pm 0.71	2.94 \pm 0.66	3.00 \pm 0.73	0.657	0.512
34	The atmosphere is relaxed during seminars /tutorials	2.67 \pm 0.98	2.61 \pm 0.91	2.68 \pm 1.0	0.522	0.6
35	I find the experience disappointing	1.89 \pm 1.01	1.95 \pm 1.03	1.87 \pm 1.01	0.604	0.547
36	I am able to concentrate well	2.70 \pm 0.94	2.44 \pm 1.06	2.78 \pm 0.88	2.596	0.01*
42	The enjoyment outweighs the stress of studying medicine	2.33 \pm 1.15	2.22 \pm 1.26	2.37 \pm 1.11	0.892	0.373
43	The atmosphere motivates me as a learner	2.73 \pm 0.86	2.66 \pm 0.84	2.75 \pm 0.86	0.799	0.425
49	I feel able to ask the questions I want	2.64 \pm 1.02	2.61 \pm 1.19	2.65 \pm 0.97	0.303	0.762

*Independent samples t-test, ($p < 0.05$ – Statistically significant)

In the domain of Students' social self-perception (SSSP) among the 7 items, 6 items were scored between 2.0 and 3.0 and 1 item was scored above 3.0. There was a significant difference across gender in response to the following item, 'There is a good support system for students who get stressed' ($p < 0.05$) and the mean overall score for this domain was (18.30 ± 3.21). Of the 50 items of DREEM inventory, 13 items were scored more than 3.0, 34 items were scored between 2.0 and 3.0 and 3 items were scored less than 2.0. Overall DREEM score among the dental students and interns is 136.09 ± 17.39 and there was no difference across gender in overall DREEM score ($p > 0.05$).

Discussion

This survey conducted using DREEM questionnaire provided an overview about the educational environment prevailing at Chettinad Dental College and Research Institute. The overall mean DREEM score was (136.09 ± 17.39) higher than the studies conducted by Betsy Sara Thomas et al (2009) at Manipal, India, where the mean score was 116 ± 0.91 for first year and 114 ± 1.12 for final year students⁸, Kamran Ali et al (2012) among dental schools in Pakistan⁹, Ostapczuk MS et al (2012) in Germany¹⁰ and Hafiza Arzuman et al (2010) in Malaysia¹¹. In the present study, the scores for all 5 DREEM subscales reflected positive perception on the institution by the students. The scores also indicated certain areas which needs further improvement in the educational environment similar to the previous studies^{8,9,10,11}.

There were 3 DREEM items that scored 2 or less. In the domain of students perception of teachers, the following negative items were scored less than 2, they are, 'the teachers ridicule the students' & 'the students irritate the teachers', the findings are consistent with the study conducted by Arzuman et al (2010) in Malaysia¹¹. Teaching in Chettinad is student-centered with periodic interaction between staff, students and parents to resolve any academic issues. In the domain of 'Students perception of atmosphere', the negative item, 'I find the experience disappointing' was scored less than 2, this was in contrary to the response to other questions in the domain which shows that the students perception about the atmosphere in the institution to be more positive and all the other items are scored more than 2.

In the present study, the institution had a student-centred teaching environment, the students were encouraged to actively participate in the class, the teaching is often simulating with emphasis on long-term learning and there is overall positive perception of learning by the students. In the domain of 'Students academic self-perception', the response to the following statement 'I am confident about passing this year' was scored higher than the study conducted by Arzuman et al (2010) in Malaysia¹¹, this is attributed to the overall positive perception of learning, perception of teachers and atmosphere prevailing in the institution.

Conclusion

The results of the present study concluded that Chettinad Dental College and Research Institute had overall a positive environment, though the

negative areas in the institution were minimal; there still exists large areas which require lots of improvement in all the subscales of DREEM.

Authors declare no conflict of interest.

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Review Article

Health Risks of Obesity

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Abstract

Obesity epidemic is taking the globe in its stride with the metamorphosed lifestyle. Obesity prevalence is constantly increasing with over a third of population being overweight or obese in India. It contributes in a big way to pathogenesis of chronic non-communicable diseases. Interventions to reduce burden of obesity, partly depend on detecting and understanding the risks complicating obesity. This article summarizes the need for focused clinical skills on obesity related health risks and vigorous validation of benefits possible through interventions toward weight management in patients.

Key Words: Obesity, Risks of Obesity, Metabolic Syndrome

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Introduction

World Health Organization has enabled the classification of individuals as overweight or obese by using a measure of Body Mass Index. Body Mass Index is calculated by dividing body weight in kilogram by square of height in meters. This is essentially the surrogate measure of body fat for specified categories of sex and age¹. A value equal to or more than 30kg/m², defines state of obesity². Different thresholds are defined by anthropometry (BMI) for overweight and obesity is stated for different ethnicity³. Prevalence of obesity increases rapidly in India. Large surveys conducted in different parts, time to time, indicate steady rising trends across all sections of population. In 2004, sample surveyed indicated 20.8% male and 32.3% female population overweight or obese. In 2007, urban males 32.4% and females 41.4% were seen as overweight or obese. Lately, in 2012, 46.6% of urban women above 35 year age and 23.7% of such rural women are overweight. Childhood and pre-pubertal obesity is also fast increasing, particularly in northern part⁴.

The distribution pattern of central obesity is, indicative of excess visceral fat. It exhibits stronger association with cardiovascular diseases than subcutaneous fat deposited around hip. Central obesity is reflected in waist circumference and the waist/hip circumference ratio. The anatomic location profoundly influences biology of adipose tissue. Increased visceral fat associates metabolic dysfunction and cardio-metabolic risk while subcutaneous fat may be protective. The two adipose tissues have embryologically different origins⁵. Visceral adipose tissue and its resident macrophages produce high quantities of proinflammatory cytokines, viz, TNF-alpha, IL-6, and low amounts of protective adiponectin. These changes in cytokines induce insulin resistance, endothelial dysfunction and consequent atherosclerosis⁶.

Mortality in Obesity

Body mass index (BMI) in excess of certain threshold for specific age/sex groups, is seen to be associated with increased mortality. Six to seven year reduction of longevity was found in a prospective observation cohort⁷. 3457 participants of Framingham Heart study were inducted at 30-49 year age. Substrata were made by sex and smoking status. Life expectancy and probability of death before 70 year age was analyzed using life table. Mortality rates specific for categories of different BMI (normal, overweight and obese at baseline/induction) and age groups were analyzed. Overweight and obesity caused large reductions in life expectancy. The follow up period was 42 years from 1948 to 1990. BMI at ages 30 to 49 years predicted mortality after 50 to 69 years, even upon adjustment for BMI at 50-69 year age⁸.

High waist (central) fat distribution increases while high fat distributed to hip decreases risk of getting myocardial infarction. It was a standardized case control study of acute myocardial infarction with 14037 controls and 12461 cases from multiple countries and ethnicities. The waist to hip ratio showed a graded and highly significant association with risk of myocardial infarction. BMI showed modest association, which disappeared when adjustments were made for waist hip ratio and other risk factors⁹.

Obesity and Diabetes

Type 2 Diabetes mellitus is the major most prevalent chronic non communicable inflammatory disease, arising as sequel to metabolic syndrome driven by insulin resistance. Overweight and obesity is found to be the main predictor of type 2 diabetes mellitus^{10,11}. During 16 year follow up of 84941 healthy female nurses, from 1980 to 1996, 3300 new cases of type 2 diabetes were detected. Overweight or obesity, as per

BMI defined cutoff constituted single most important predictor of diabetes development¹⁰. Data from cohort of 51529 US male health professionals in age range 40-75 years in 1986 was analyzed following 5 year follow up, in 1992. Persons developing NIDDM numbered 272. Strong positive association of obesity defined by BMI and risk of diabetes development was demonstrated¹¹.

Mechanistic links of obesity to diabetes development are hypothesized with partial supportive observations. Genetic and epigenetic predisposition for preferential deposition of fat in abdominal depots is proposed. This process may be added by stress induced hypothalamo-pituitary-adrenal axis activation. The overflow of uncontained fat from omental and mesenteric tissue probably invades organs as liver, skeletal muscles, inflicting metabolic dysfunction. Direct effect of omental and mesenteric adipose tissue depots may be exerted on insulin resistance, lipoprotein metabolism and blood pressure. Metabolic products of omental and mesenteric adipose tissue depots are released in to the portal vein, which provides direct delivery to liver. Lipolysis of omental and mesenteric adipose tissue triacyl-glycerol releases free fatty acids that can induce hepatic insulin resistance and provide substrate for lipoprotein synthesis and neutral lipid storage in hepatocytes. In addition, specific proteins and hormones produced by omental and mesenteric adipose tissue, such as inflammatory adipokines, angiotensinogen and cortisol (generated by local activity of 11 beta hydroxysteroid dehydrogenase), can also contribute to cardio-metabolic disorder¹².

Hypertension and Obesity

Obesity increases risk of developing hypertension^{13,14}. In a large study, 14924 adult participants were grouped by BMI cutoffs and waist circumference as per NIH criteria. Relative risks of hypertension, dyslipidaemia and metabolic syndrome were higher in overweight and obese. These risks correlated positively with waist circumference. Importantly, risk level associating a given waist circumference was unaffected by differences in BMI, emphasizing major significance of the parameter¹⁵.

Obesity and Heart Disease

Number of studies have established regular relation of obesity to increased risk of coronary artery disease^{14,16}. The obese are also twice as likely to suffer heart failure as the non obese¹⁷. Paradoxically, the survival rate of obese heart failure cases is better than the non obese¹⁸.

Obesity and Cerebrovascular Disease

Increased BMI associates increased risk of ischemic stroke. Hemorrhagic stroke risk appears to concentrate at either extremes of the BMI¹⁹. Lean body weight and lower cholesterol level have been linked to increased hemorrhagic stroke risk by a prospective cohort of 21414 male physicians²⁰. During 12.5 years of follow-up, 747 strokes (631 ischemic, 104 hemorrhagic, and 12 undefined) occurred. Compared with participants with BMIs less than 23, those with BMIs of 30 or greater had an adjusted relative risk of 2.00 (95% confidence

interval [CI], 1.48-2.71) for total stroke, 1.95 (95% CI, 1.39-2.72) for ischemic stroke, and 2.25 (95% CI, 1.01-5.01) for hemorrhagic stroke. When BMI was evaluated as a continuous variable, each unit increase of BMI was associated with a significant 6% increase in the adjusted relative risks of total (95% CI, 4%-8%), ischemic (95% CI, 3%-8%), and hemorrhagic stroke (95% CI, 1%-12%). Additional adjustment for hypertension, diabetes mellitus, and hypercholesterolemia slightly attenuated the risks for total and ischemic (relative risk 4%; 95% CI, 2%-7%), but not hemorrhagic, stroke. Another study was conducted in Korea, on 2,712 persons (904 cases, 904 hospital controls, and 904 community controls)²¹. Obese men ($25.0 \leq \text{BMI} < 30.0 \text{ kg/m}^2$) had an odds ratios (OR) of 1.39 (95% CI 1.03 to 1.87) a hemorrhagic stroke, compared to men with a normal BMI (18.5 to 24.9 kg/m^2). Conversely, women with lower BMI had a higher risk of having hemorrhagic stroke. About a three-fold increase was observed in the risk of intracerebral hemorrhage (ICH) in the highly obese group obesity was identified as one of the risk factors in hemorrhagic stroke, in particular ICH. Conversely, in women, a lean body weight increases the risk of hemorrhagic stroke. Consequently, managing one's weight is essential to reduce the risks of hemorrhagic stroke. Central (truncal) obesity increases stroke related mortality, however²².

Role of Obesity in Metabolic Syndrome

Metabolic syndrome is defined by presence of any three the following five features: viz. 1) waist circumference above 40 inches in male and 35 inches in female; 2) triglyceride level above 150 mg/dl; 3) High Density Cholesterol (HDL) level below 40mg/dl in male or 50mg/dl in female; 4) Blood pressure above 130/85 mmHg; and 5) Fasting blood glucose level above 100mg/dl²³. The altered lipid and glucose metabolism appears to be consequent to central obesity and insulin resistance.

Obesity and Pulmonary Abnormality

Obesity and accompanied increased neck circumference is found to strongly link to the obstructive sleep apnea²⁴. Increased fat tissue may impinge upon airway lumen increasing collapsibility²⁵. Obesity also increases asthma risk and majority of asthmatic emergency cases are found to be obese or overweight²⁶. Obesity asthma linkage may involve decrease in functional and tidal volume, chronic state of sub-acute systemic inflammation including increased production of mediators and the increased hyper responsiveness of airway²⁷.

Obesity and Gastrointestinal Disorders

Obesity is significantly associated to gastro esophageal reflux disease and its late sequel as erosive esophagitis, esophageal cancer etc²⁸. Obese men and women both suffer increased incidence of gall stones^{29,30}.

Obesity and Reproduction Disorders

Obesity and insulin resistance typically associate the polycystic ovarian disease that exhibits anovulation and hyper-androgenism. Weight loss and therapeutic remediation of insulin resistance can reverse anovulation and aberrant hormonal profile in these

patients³¹. Obesity negatively impacts male sexual function and fertility, with recovery benefit of weight reduction³². Gestational diabetes is likewise more prevalent in the obese with predictable diverse complications for mother and baby³³.

Obesity and Late Age Health

Osteoarthritis ensues upon obesity³⁴. Besides the extra strain on weight bearing joints, there is evidence of systemic dysregulation of adipokines, to explain increased osteoarthritis in the obese people³⁵. Increased incidence of certain cancers in the obese is reported, viz. cancers of gall bladder, esophagus, thyroid, kidney, uterus, colon, breast etc³⁶. A lean body weight is known to reduce both incidence and mortality of the cancers^{37,38}. Cancers of reproductive and secondary sex organs in females may draw boost from high estrogen synthesis from increased fat³⁹. The evidences are most consistent for endometrial cancer, breast cancer among the postmenopausal women, and renal cell cancer. The molecular mechanisms linking obesity to increased cancer incidence have been poorly understood.

Obesity & Health Related Quality of Life

Several neuropsychiatric maladies like somatization, hypochondriasis, phobias, and obsessive compulsive disorders have shown amelioration in obese patients after undergoing bariatric surgery⁴⁰. Many surgical procedures in the obese carry poor prognoses due to associated ill health. Obesity evidently would increase immobility and access to proper health care.

Conclusion

Thus, given the magnitude of complications related to obesity, addressing this linkage and revelation of diseases linked to obesity constitute, vital facets of clinical competence and quality care.

Authors declare no conflict of interest.

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Class Room

Surgeries for End Stage Heart Failure

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Introduction

Heart failure (HF) is a leading cause of death nowadays. Heart failure is a pathophysiologic condition that leads to inadequate cardiac performance and is responsible for the heart's inability to increase output. The myocardium responds to the reduced output by compensatory mechanisms of the Frank-Starling relationship¹, ventricular wall thickness, ventricular geometry, and neurohormonal activation. The neurohormonal system stimulates a cascade of hemodynamic alterations that adversely affect outcome².

Neurohormonal system activation leads to further cardio myocyte dysfunction and endothelial dysfunction that leads to abnormal hemodynamics. Neurohormonal activation leads to hypertrophy and remodeling of the ventricular chamber resulting in the progression of the HF³.

When myocardium is damaged, its ability to maintain adequate cardiac output decreases. A subnormal heart leads to sluggish circulation (congestion) and results in fatigue, shortness of breath, pedal oedema and irregular heart-beats. Common causes of heart failure are ischemic heart disease, myocardial infarction, hypertension, valve disease, muscular dysfunction and arrhythmias.

After myocardial injury the heart remodels and dilates, an increase in wall tension occur secondary to increased radius of curvature, as per Laplace's law leading to increased myocardial oxygen consumption, decreased sub-endocardial blood flow, impaired energetic, and increased arrhythmias. Poor prognosis directly correlates with the degree of remodeling. Pharmacologic therapy leads to some improvements to ventricular function and long term results, however the improvement in frequently inadequate⁴.

Heart failure is associated with long hospital stay, multiple readmissions, and reduced quality of life. In patients with HF secondary to systolic dysfunction, the primary objectives of therapy are to improve survival, alter disease progression, and reduce symptoms. Pharmacologic treatment include the blocking of neurohormonal responses. Pharmacologic therapy results in improved left ventricular (LV) function¹.

Surgical management of patients with end-stage, refractory systolic HF are limited. Heart transplantation remains the optimal treatment for end-stage HF. Contraindications due to recipient co morbidities, and transplant complications preclude routine use. Heart transplantation is not an option for majority of patients.

Other surgical approaches to end-stage HF includes:

- Coronary Revascularization with ischemic cardio myopathy.
- DOR Procedure (Fig 1).
- Mitral valve repair (Mitral Regurgitation correction) with dilated cardiomyopathy.
- Left ventricular assist devices (LVADs) (Fig 2).

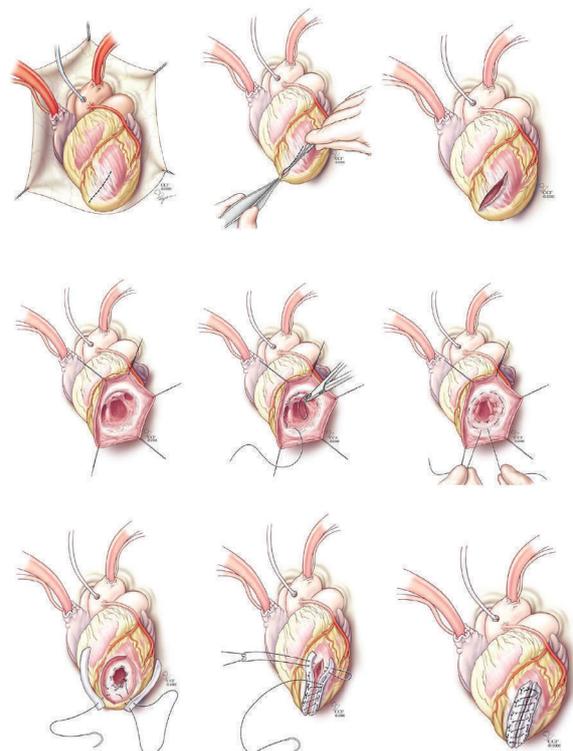


Fig 1 - DOR Procedure

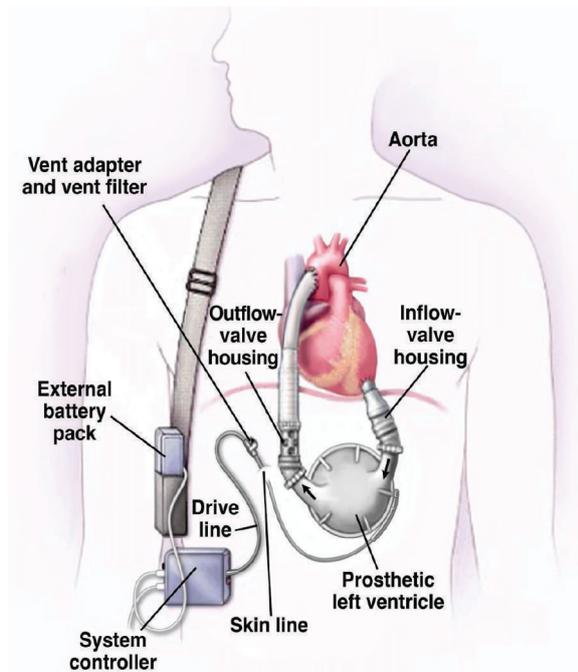


Fig 2 - Schematic view of a cardiovascular system with an LVAD

A. Coronary Revascularization with ischemic cardiomyopathy

Ischemic cardiomyopathy is significantly impaired left ventricular function (left ventricular ejection fraction \leq 35 to 40 percent) that results from ischemic heart disease.

Ischemic cardiomyopathy is a condition initiated by primary events in the coronary circulation that lead to myocyte loss, scarring, and ventricular failure. Cell loss occurs as a result of narrowing or occlusion of coronary arteries by atherosclerosis, spasm of major arterial branches of the coronary vasculature, or alterations of the microcirculation, which, alone or in combination, produce varying degrees of ischemia and myocardial injury⁵.

The clinical spectrum ranges from myocardial infarction to chronic ischemic cardiomyopathy. The latter is a form of dilated ischemic myopathy characterized by multiple focal sites of myocardial damage in the ventricular wall⁶.

Patients with HF who are at risk for ischemic heart disease should be screened for myocardial ischemia. Revascularization, through either percutaneous or a bypass surgery, often improves symptoms, improves cardiac performance, and reduces the risk of sudden death⁷.

Viability testing has a role in identifying patients who are unlikely to benefit from revascularization⁸. Revascularization was proposed as the treatment of choice in the advanced HF patients with ischemic cardiomyopathy, a LVEF below 35%, viable myocardium and vessels suitable for grafting⁹.

CABG has good long-term outcome in angina free patients with ischemic cardiomyopathy and heart

failure who have residual viability. However, associated diastolic impairment, reflected by elevated left ventricular end-diastolic pressure (LVEDP), predicts reduced long-term survival despite myocardial viability⁸.

Patients with ischemic cardiomyopathy and viable myocardium, revascularization surgery is not a new but an established treatment concept. Concerning the assessment of viability, it is of utmost importance to predict regional functional recovery. Patients with ischemic cardiomyopathy will remain the recipients of on- and off-pump CABG as surgical techniques and medical therapies continue to improve¹⁰.

The future of revascularization in these patients will focus on improving results and making CABG for elective revascularization less invasive and safer.

B. DOR Procedure

LV aneurysmectomy has been offered as an option for the patients with symptomatic aneurysms that have been defined as including those associated with HF, angina pectoris, systemic embolization, and/or malignant ventricular tachyarrhythmias. The Dor procedure, also called endoventricular circular patch plasty (EVCPP) or endoventricular patch reconstruction, is an approach to surgical reconstruction in the setting of post-infarction aneurysm formation¹¹.

A dilated left ventricle is generally due to remodeling secondary to myocardial infarction. Occlusion, results in either akinetic (non-beating) or dyskinetic tissue. This tissue is virtually useless. However, the end-diastolic volume, remains constant, so the tissue that still functions has to do more work to eject the blood.

If the cardiologist determines that the Dor procedure is necessary, then the patient must have symptoms to show that they would be a good candidate, either, angina, heart failure, arrhythmias or a combination of the three, areas of akinesis or dyskinesis and ejection fraction of $<40\%$. This surgery is performed following a coronary artery bypass graft (CABG)¹².

Contraindications include impaired right ventricular function, pulmonary hypertension, basal dysfunction, systolic pulmonary artery pressure greater than 60mmHg¹².

Dor procedure overcomes the problems related to linear suture excluding the septal extension of myocardial scar from the ventricular chamber, diverting myocardial fibers toward the apex, decreasing the tension on the transitional zone, and aiding the revascularization of the LAD. In a study done by Di Mattie DG et al., concluded that functional and clinical status is improved late after operation in the majority of patients where endoventriculoplasty of LV aneurysm and coronary grafting was done. Patients who benefit most from the operation were those with a normal postoperative contraction pattern, where ejection fraction improved¹³.

C. Mitral Regurgitation Correction

Another harmful effect of remodeling is mitral regurgitation. Mitral re-gurgitation (MR) frequently complicates cardiomyopathy (CM) and results in congestive symptoms¹⁴. Severe mitral regurgitation is a complication of end-stage cardiomyopathy that predicts poor survival⁹.

As the left ventricle dilates the heart assumes a globular shape, the papillary and mitral complex alters, causing restricted opening and due to tethering of the leaflets and distortion of the mitral apparatus. Increasing ventricular dilation results in mitral annulus dilatation. Mitral regurgitation causes a volume overload of the left ventricle that contributes to remodeling and progression of disease. Correction of mitral regurgitation is recommended⁷.

The basic principle of the surgical treatment of functional MR is to restore coaptation of the mitral leaflets by reshaping the mitral annulus with reduction of the septolateral distance, so that the anterior mitral leaflet covers the complete orifice of the mitral valve¹⁵. The complete and rigid annuloplasty rings ensure better outcomes than partial and flexible rings^{16,17}.

Ischemic MR is associated with a poor prognosis, but there is no substantive evidence that the regurgitant lesion per se causes the poor outcomes and surgical correction of MR at the time of coronary artery bypass grafting has little effect on survival¹⁸. Treatment of chronic ischemic MR includes medical therapy for heart failure, cardiac resynchronization therapy and possibly mitral valve surgery or heart transplantation.

D. Heart transplantation

Heart transplant is curative for chronic HF, the survival rate is approximately 50% at 10 years¹⁹.

Indication for heart transplantation are HF, angina and arrhythmias refractory to medical therapy. Severe angina in the absence of HF is not a indication for transplantation. Intractable ventricular arrhythmia are often urgent listing for mechanical support or transplant²⁰.

Contraindications for transplantation are medical or psychological. Most of these are relative contraindication and are considered with relation to the HF. The medical contraindications are age, obesity, malignancy, pulmonary hyper-tension, diabetes, renal dysfunction, peripheral vascular disease and infection. Timing of transplant referral is the greatest challenge for a cardiologist²⁰.

E. Left ventricular assist devices - LVADs

A left ventricular assist device (VAD, also called ventricular assist system or VAS) is a type of mechanical circulatory support device (MCS). It is a mechanical pump that is implanted in patients who have heart failure to help the heart's weakened left ventricle (major pumping chamber of the heart) pump blood throughout the body.

The evolution of mechanical circulatory assist devices,

aimed to bridge the heart to transplantation, or to myocardial recovery, has helped many of patients. Nowadays, these devices are even implanted for long-term support (Destination Therapy), particularly in elderly patients and in those with contraindications to heart transplantation. This may even be the best and the optimal solution to treat heart failure patients in the future²¹. The LVAD will provide blood pressure support; and improve organ function by increasing blood flow.

In unstable patients with end stage HF who are unsuitable for LVAD, a total artificial heart can be used as a bridge to transplantation and this improves survival to transplant and post transplant²². Elective bridge to transplantation was found to be associated with better survival than emergency implantation of assist devices²².

This has become essential in the face of the increasing donor organ shortage, with many patients receiving permanent assist devices and fewer receiving heart transplants. Various assist systems are now able to improve physical conditions and offer the patient good quality of life for several years. This is also true for patients with contraindications for heart transplantation²¹.

Authors declare no conflict of interest.

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Class Room

How to Write a Paper

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Introduction

Publishing in peer reviewed journals is the hallmark of an accomplished doctor. As doctors, we have 3 responsibilities – to our patients by upholding the highest standards of care, to future generations of doctors by teaching them and to our profession by sharing our knowledge and experience. Publication of the results of clinical work and reviewing the results of studies published by others is the result of and proof of critical independent thought. These activities demonstrate that the author who is a doctor is not only capable of following e.g. I do because my chief told me so, but of being a leader – I do because I have analysed the evidence and the evidence shows so. But why is it important to think critically?

Well, only 150 years ago, a doctor called Semmelweis was taken to task for advocating hand washing between patients! At the time doctors would work between autopsy rooms and obstetric delivery rooms without bothering to wash their hands. Semmelweis observed and published on the fact that doctor - led obstetric delivery units had several fold puerperal sepsis rates as compared to midwifery - led units. He advocated hand washing and as a result, saved the lives of many mothers and babies¹. For making the link between dirty hands and puerperal sepsis, he was made an outcast! Semmelweis was committed to an asylum, where he died at a young age. More recent events include the thalidomide scandal and the autism link with MMR immunisation. In my opinion, the medical profession has one guardian angel – and that is the critical evaluation of data. Greater academic enterprise, critical analysis of results and academic research are therefore critical for a specialty to progress and a doctor to demonstrate to his/her peers that they are capable of good quality work. Of course, on a more practical note, academic institutions in the United States for instance mandate that the attending doctors (senior consultants) publish. This attracts patients and popularises the institution – so publishing papers can have a positive effect on the profile of the institution as well.

Defining the research question

The most important aspect of writing a paper is defining the research question. Framing a good question – one that will interest the reader and be worthy of investigation is the key to a good paper. A research question should be framed in the PICO or the PECO format; Patient – define the patient group,

Intervention or investigation - what is the intervention or investigation being evaluated, Comparator – what is the intervention or investigation being compared to and Outcome – what outcomes are defined as being of interest. Clearly defining each of these categories enables a well conducted study as well as clarity of presentation of results. The PICO/PECO also enables careful consideration of the most appropriate study design. Interventions are best evaluated in a randomised controlled trial; tests can be evaluated in a single arm prospective diagnostic test accuracy study, complex risk exposures are best assessed in a cohort study. Good online resources exist to guide study design selection and presentation (see www.cebm.net.) Dedicated courses (www.publishingclinic.co.uk) can help guide publication.

The null hypothesis and statistics

Deriving a hypothesis is helpful to calculate the numbers needed – usually the null hypothesis states that the new treatment is no different from the existing treatment for the defined outcomes. The study sample size then has to derive the number of treatment effects that are needed to demonstrate that the null hypothesis is disproved. A statistical expert may be helpful for this. Free web resources are also available (<https://www.sealedenvelope.com> and <https://www.youtube.com/watch?v=g3dkRsTqdDA>). Youtube also has some excellent tutorials on statistical tests. So let's assume that the research project is completed and the results need to be written up for publication. How does one get started?

Getting started

The figures and tables of the study are the best place to start. Collating the data into tables and the results into graphs for figures helps defining the results section of the manuscript. Figures should be labelled legibly, with clear legends and titles. Interestingly, it allows for reflection as well – do the results prove or disprove the hypothesis. Often, results of single institution experiences are not adequate to do either – hence the need for collaboration between institutions to generate large multicentre datasets for definitive conclusions. However, single institution case series can be extremely helpful as a starting point - the data may show a trend towards a significant result which may need to be proved in larger studies.

Choosing a title and targeting the most appropriate journal

The next step is to choose a title. There is a balance to be struck between short catchy titles that don't describe the study in anyway – e.g. Cervical cancer in India – the title doesn't make clear whether this is a narrative review or a randomised controlled trial and long unwieldy titles – e.g. A systematic review of factors affecting outcomes after treatment with antagonists of tumour necrosis factor- α in patients with rheumatoid conditions. Some journals have criteria for Titles and will provide clear direction to authors on the correct titles for the journal of choice.

This is a good time to select the journal of choice. It is advisable to select a first choice, second choice and a third choice journal. Most good journals have an acceptance rate of less than 10% - so it's pragmatic to aim slightly higher and use the reviewer feedback to hone the paper if needed. Is this journal interested in the kind of research that has been undertaken? One easy tip is to check through the papers that have been selected as references to see where they have been published. This allows for target journals to be identified. Understanding the importance of impact factor helps – the impact factor is a score published by the journal publishers which is an average of the number of times a paper published in the journal is cited i.e. referenced in another paper. The higher the Impact factor, the more significant the journal is considered to be. Impact factors range from the 35+ (Cell/Nature/Science/Lancet) journals to the very low.

Having said that, specialty journals tend to have lower impact factor reflecting the pool of readership – Obstetrics and Gynaecology (Green journal) the highest ranking journal in Obstetrics and Gynaecology has an impact factor of 4.3. Most doctors or medical students will start with publishing in institutional journals. These are useful stepping stones to national and then international publications. Nevertheless, the key is that once the target journal has been identified, the instructions are to be followed very carefully. This is one instance when 'following the rules' does pay!

The IMRAD format

Most research articles are written in the IMRAD format – Introduction, Methods, Results and Discussion². The Introduction sets the scene for the research question and is usually no more than 50 words. The Methods and Results section are perhaps the most important sections of the manuscript. The Methods should be straightforward to write if the study design has been selected after careful consideration. www.equator.net is a very useful site for this section and has compiled the relevant guidelines for each study design. Some journals will ask for a checklist to be completed to demonstrate that the relevant guidelines have been followed for each study type – e.g. PRISMA for systematic reviews, CONSORT for trials etc.

Results need to be a factual presentation - the interpretation of results is left to the discussion section. Again, this is presented in a concise fashion. Usually most

research papers will stipulate no more than 6 figures and tables, with the text in the results describing in detail the data presented in the figures and tables. Usually, most academic papers expect 3 results to be provided – ie the study showed that treatment x as compared to treatment y in the population of interest improves progression free survival (result 1), is associated with similar complications (result 2) but has a higher impact on patients quality of life (result 3).

The Discussion section provides the interpretation of the results. This section places the results in context, discusses the strengths and limitations of the study and suggests any impact on clinical practice as well as suggestions for future research. Journal editors will ask themselves three questions of each manuscript – are these results generalisable, valid and applicable?. The conclusion section is a balancing act – unless the study is a multicentre definitive randomised controlled trial, its best to show some caution in the interpretation of study findings. For instance, a conclusion might read 'In this pilot study outcomes from Robotic surgery were atleast comparable with laparoscopic surgery, with a trend towards reduced hospital stay. These findings need confirmation in a well designed larger trial'.

Tips and Tricks

It is a good idea to ask colleagues to review the paper before submission – one tip is to ask a colleague in an allied specialty to read the manuscript e.g. an anaesthetist for a surgical manuscript. If the paper is written with clarity, the colleague should be able to understand and convey the principles underlying the paper. Paying attention to language helps. Most international journals prefer concise language without flowery embellishment, for instance, 'conclusively show' is better than 'show without a shadow of doubt'. Of course, the spell-check function on the computer and remembering that American publishers insist on American English spelling is important.

Finally, writing and publishing papers takes time and practice. In my experience, it takes about 6 months from writing up through to submission and publication. Starting from a first draft through to submission will occupy precious hours of time. Remember also that rejection is very common – editors in reputed journals accept <10% of submissions. Others have faced rejection too - the manuscript describing the link between *H.pylori* and gastric cancer was rejected several times! Do use the reviewer's feedback to improve the submission and try again. Rest assured, seeing one's name in print and the results of hard work published and acknowledged by peers is worth it!

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Editorial note

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The 'Vancouver' protocol was first laid down in 1978 by an informal meeting of a group of Medical journal editors in Vancouver, British Columbia. This group has now evolved into the International Committee of Medical Journal Editors (ICMJE), which meets annually and presents periodically revised Uniform requirements for manuscripts submitted to biomedical journals.

Authorship - credit should be based on:

- Contributions to conception and design, acquisition of data, or analysis and interpretation of data
- Drafting the article or revising it critically
- final approval of the version to be published

However general supervision of the effort does not constitute authorship. It is recommended that the editorial freedom involves full authority over the editorial content and timing of publication.

When a study involves use of a drug, commercially available equipment or a trademarked test kit, it is the responsibility of the author to disclose all financial and personal relationship with the concerned company. If financial support is availed of, the study design, execution, analysis and results should be independent of the finance source and should be kept private. Reviewers should disclose financial and personal affiliation with regards to the reviewed study. Duplicate publication in two journals, redundant publication with repetition of data and results should be avoided at all cost.

Manuscript Preparation and Submission

The sections should be divided into the IMRAD format, introduction, methods, results and discussion. All portions of the manuscript should be double spaced and serially numbered. Case reports, 'how to do it' articles, correspondence, editorials and perspectives do not require an abstract.

Cover letter : The cover letter should state the purpose of the study and why it is important. It also states the participation of all the authors, originality of the work and conflict of interest if any.

Title page : The title page should include a title that describes the study in a concise manner as possible. Abbreviation and long convoluted titles should be avoided. The authors name, designations, departmental and institutional affiliations should be clearly stated. The contact information for the corresponding author should appear clearly. Word count, number of figures, tables, pages, and keys words should be included. A concise 100 word write up on the first author with a passport size photograph should be included.

Abstract : The abstract should follow the IMRAC format with introduction, methods, results and conclusion. It should not exceed 250 words. Abbreviations are generally avoided in an abstract.

Introduction : The introduction should be brief and focused and should contain a background to the study in question and hypothesis to be tested with relevant references.

Methods:

- This section is important and should include
- Time duration and location of study
- Institutional review / ethics committee approval (review articles and case reports can dispense with approval)
- Patient demographics – this is best presented with tables. with texts noting only the submit points.
- Details of inclusion and exclusion criteria
- End points both primary and secondary should be stated with description of statistical method used.
- Technical details of the clinical procedures and investigations, questionnaires should be described with focus.

Results

The results section is best presented with graphs and tables. long lengthy paragraphs with numerous figures and numbers should be avoided. Salient findings can be described with significance, in brief. Repetitions of data from table should be avoided.

Discussion & References

The discussion itself must be structured to lend clarity to the reader. Most discussion are begun by reiterating the background, historical details of the device or procedure and epidemiological data. Following which data from similar literature on the subject of the study is detailed impartially with minimal reference to current study, highlighting similarities or contrast. The application of the result to the general population needs to be discussed.

Always follow this with the small description of the limitations, drawbacks and biases and make short, concise, clear conclusions. References from journals and books should be formulated as per guidelines set by the Vancouver group. References should be to the point and relevant to the study. There is no requirement for numerous references unless it is a review article.

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Editorial note

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When a study involves use of a drug, commercially available equipment or a trademarked test kit, it is the responsibility of the author to disclose all financial and personal relationship with the concerned company. If financial support is availed of, the study design, execution, analysis and results should be independent of the finance source and should be kept private. Reviewers should disclose financial and personal affiliation with regards to the reviewed study. Duplicate publication in two journals, redundant publication with repetition of data and results should be avoided at all cost.

Manuscript Preparation and Submission

The sections should be divided into the IMRAD format, introduction, methods, results and discussion. All portions of the manuscript should be double spaced and serially numbered. Case reports, 'how to do it' articles, correspondence, editorials and perspectives do not require an abstract.

Cover letter : The cover letter should state the purpose of the study and why is it important. It also states the participation of all the authors, originality of the work and conflict of interest if any.

Title page : The title page should include a title that describes the study in a concise manner as possible. Abbreviation and long convoluted titles should be avoided. The authors name, designations, departmental and institutional affiliations should be clearly stated. The contact information for the corresponding author should appear clearly. Word count, number of figures, tables, pages, and keys words should be included. A concise 100 word write up on the first author with a passport size photograph should be included.

Abstract : The abstract should follow the IMRAC format with introduction, methods, results and conclusion. It should not exceed 250 words. Abbreviations are generally avoided in an abstract.

Introduction : The introduction should be brief and focused and should contain a background to the study in question and hypothesis to be tested with relevant references.

Methods:

- This section is important and should include
- Time duration and location of study
- Institutional review / ethics committee approval (review articles and case reports can dispense with approval)
- Patient demographics – this is best presented with tables. with texts noting only the submit points.
- Details of inclusion and exclusion criteria
- End points both primary and secondary should be stated with description of statistical method used.
- Technical details of the clinical procedures and investigations, questionnaires should be described with focus.

Results

The results section is best presented with graphs and tables. long lengthy paragraphs with numerous figures and numbers should be avoided. Salient findings can be described with significance, in brief. Repetitions of data from table should be avoided.

Discussion & References

The discussion itself must be structured to lend clarity to the reader. Most discussion are begun by reiterating the background, historical details of the device or procedure and epidemiological data. Following which data from similar literature on the subject of the study is detailed impartially with minimal reference to current study, highlighting similarities or contrast. The application of the result to the general population needs to be discussed.

Always follow this with the small description of the limitations, drawbacks and biases and make short, concise, clear conclusions. References from journals and books should be formulated as per guidelines set by the Vancouver group. References should be to the point and relevant to the study. There is no requirement for numerous references unless it is a review article.

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Case Report

Clinicopathologic Case Report of Retrosternal Goitre

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Key words : Retrosternal Goitre, Tracheal compression, Non- resolving pneumonia

Chettinad Health City Medical Journal 2015; 4(1): 43 - 45

Case summary

A 60 year old male patient was transferred to our hospital with a diagnosis of community acquired lobar pneumonia and scrub typhus. He was a diabetic and hypertensive and was also positive for the HbsAg antigen. He was being treated with mechanical ventilation for respiratory failure and antibiotics for pneumonia and scrub typhus. His general condition, sepsis and respiratory status gradually improved. He was taken off mechanical ventilation on the second day following admission to the intensive care unit; however he developed an inspiratory stridor and respiratory distress for which he was put back on

mechanical ventilation. CT scan of the thorax showed an anterior mediastinal mass contiguous with the lower lobe of the thyroid, compressing the trachea and extending behind the arch of the aorta (fig 1 & 2). The lung windows were consistent with diffuse pneumonic changes with bilateral small pleural effusions. He underwent surgical resection and a subtotal thyroidectomy through a collar incision and a upper hemi- sternotomy. The mass was confirmed to be a colloid Goiter (Fig 3).He was weaned off the ventilator in 12 hours and was discharged home on the eighth postoperative day.



Fig 1 - Sagittal view of thyroid mass compressing the trachea

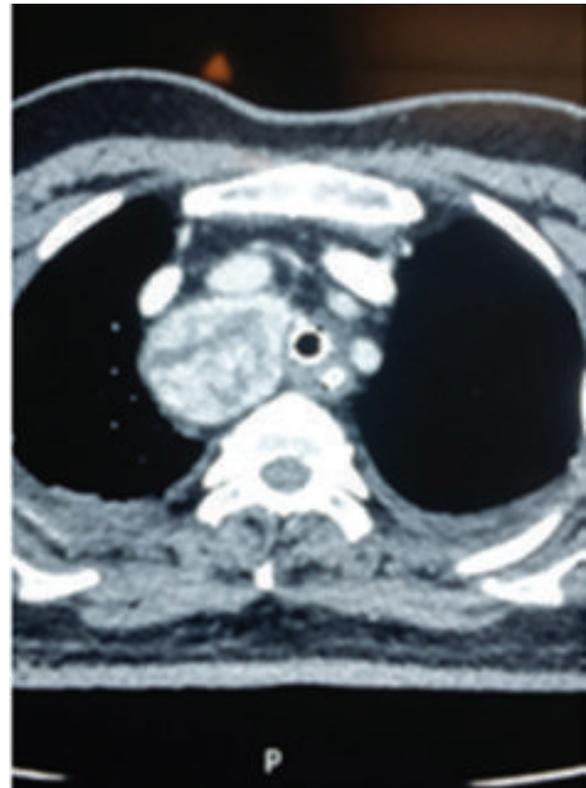


Fig 2 - Coronal view of thyroid mass compressing the trachea

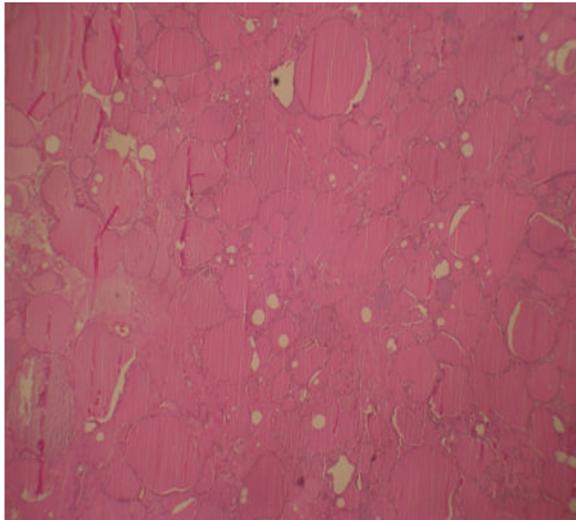


Fig 3 - Photomicrograph of haematoxylin and eosin stained sections showing Thyroid follicles of varying sizes filled with colloid (4X10X).

The absence of toxemia and minimal pleural effusion, ruled out abscess, empyema. Echocardiography ruled out endocarditis. Sputum AFB and other cultures ruled out tuberculosis and fungal infections.

Malignancy, pulmonary embolism, systemic inflammatory disorders were systematically ruled with a combination of history, lower limb Doppler and appropriate immunological blood investigations (Fig4).

The CT scan confirmed the presence of a mass lesion compressing the trachea that explained the difficulty in weaning the patient off ventilator support (Fig 1 & 2).

- In a patient with unresolving or slowly resolving pneumonia, unusual causes and unusual organisms are suspected only after treatment failure.
- A systematic approach to ruling out all causes will prevent life threatening situations

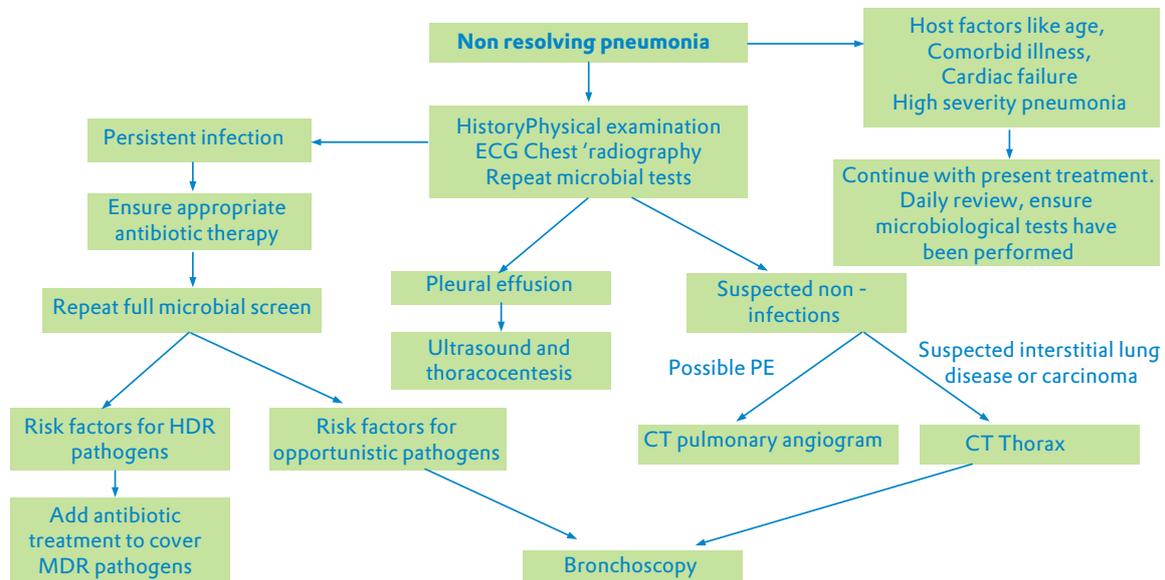


Fig 4 - An algorithm for the investigation and management of non-resolving pneumonia.

Discussion

Intensive care perspective

Differential diagnosis of non resolving pneumonia

1. Complications of pneumonia like empyema or abscess
2. Infective endocarditis
3. Host factors such as old age, alcoholism, immunosuppression and multilobar pneumonia
4. Unusual organisms like tuberculosis, fungi, multi drug resistant pathogens
5. Malignancy or mass lesion with airway obstruction
6. Systemic inflammatory disorders such as SLE, Wegener's granulomatosis etc
7. Drug induced lung disease
8. Pulmonary embolism with infarct

- Rare causes of mass lesions compressing the airways should prompt the clinician to consider more exhaustive imaging techniques.

A surgical and pathological perspective

Differential diagnosis of a mass in the anterosuperior mediastinum.

1. Thymic neoplasms
2. Thyroid and parathyroid neoplasms
3. Lymphomas
4. Germ cell tumours
5. Thoracic aortic aneurysms

A goiter that extends beyond the thoracic inlet is termed a retrosternal goiter¹. Retrosternal goiters are rare, they are extremely difficult to diagnose if they are

confined to the mediastinum. The incidence varies from 0.02-0.5% in a chest X ray screening series².

The differential diagnosis should include thymic tumours and lymphomas, these are significantly more common in the antero-superior mediastinum. Presenting symptoms are diverse and include, shortness of breath, dysphagia, hoarseness of voice and stridor³, however contrary to popular belief tracheomalacia is uncommon.

The common surgical approaches include a cervical collar incision, upper sternotomy, full sternotomy and rarely lateral thoracotomy⁴.

Learning Points

- Retrosternal goiters can be approached through a variety of incision, the ideal incision should give good access for a complete resection.
- Tracheomalacia is extremely rare⁴
- Malignancy in a retrosternal goiter is rare (2-3%)
- A mass attached to the thyroid is most likely a retrosternal goiter⁵
- Ectopic thyroid present in the anterior mediastinum may result in a retrosternal goiter and blood supply is derived from mediastinal vessels⁶

Conclusion

Retrosternal goiters can present with obstructive symptoms and pneumonia. A systematic approach is required to make an early diagnosis to prevent further patient morbidity, surgical approach should be tailored to the size and location of the goiter.

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Case Report

Concomitant Repair of a Giant Bochdalek Hernia With Coronary Artery Bypass Grafting

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Key words : Bochdalek Hernia, Coronary Artery Bypass Grafting

Introduction

Congenital diaphragmatic hernias resulting from the failure of posterolateral diaphragmatic foramina to close, was first described by Bochdalek in 1848¹. Presentation in adults is rare, usually they present with mild respiratory or gastrointestinal symptoms¹. We present an adult patient who underwent simultaneous coronary artery bypass grafting and hernia repair through a median sternotomy. There have been no similar reports of combined procedure.

Case Report

A 42 year old patient, diagnosed to have coronary artery disease after having an anterior wall Myocardial Infarction, presented to us with history of recurrent angina and dyspnea on exertion NYHA class III. His chest x ray (fig.1a & 1b) showed bowel loops occupying the right lower and middle zones with cardiomegaly. Computed tomography confirmed the presence of a Bochdalek hernia with herniated bowel loops and mesocolon (fig 2 & 3). He underwent coronary Angiography that showed completely occluded left anterior descending artery. His vitals were normal and blood work up was within normal limits. On examination, bowel sounds were heard across the entire right hemothorax.

He was taken up for surgery. A double lumen endotracheal tube and monitoring lines were inserted. He underwent coronary artery bypass grafting using the off pump technique, using a suction stabilizer device and mister blower through a median sternotomy. After completion of the left internal thoracic artery to left anterior descending artery bypass, the chest retractor was removed and an internal mammary artery harvesting retractor was used to elevate the right hemisternum, to aid exposure to the right posterolateral recess. The right lung was collapsed by clamping the double lumen endotracheal tube. Bowel loops and mesocolon were seen enveloped by a thin peritoneal layer. A large 5x5 cm defect was found in the right posterolateral recess. The hernia was reduced and the defect was closed with a polypropylene mesh using 4-0 polypropylene sutures. Patient made an uneventful recovery and was discharged on fourth post operative day.



Fig 1a: Pre op Chest X-ray showing bowel loops occupying the Right lower and middle zones with cardiomegaly



Fig 1b: Post op Chest X- ray showing small pleural effusion and clear lung fields

Discussion

Bochdalek hernias were described in 1848¹. They occur due to failure of the pleuroperitoneal canal to close during the tenth week of gestation². They normally present in early infancy with severe respiratory symptoms³. They are usually asymptomatic in adults, but older patients can present with mild respiratory and gastrointestinal symptoms. The incidence in adults is estimated to be about 0.17%⁴.

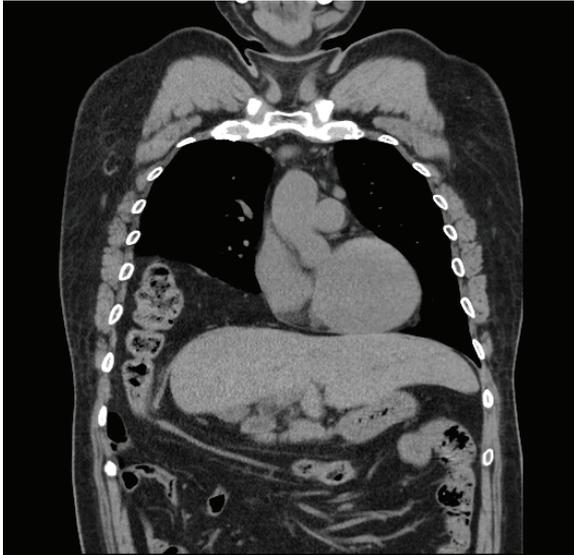


Fig 2: Coronal view showing bowel loops and mesocolon in right thorax



Fig 3: Sagittal view showing bowel loops and mesocolon in right thorax

Gopala Krishnan et al have described a combined morgagni hernia repair with coronary artery bypass surgery, as the hernia is located in the middle mediastinum, access through a median sternotomy is ideal⁵, a Bochdalek hernia however is not easy to access though a sternotomy due to its lateral and posterior location.

Repair of Bochdalek hernias can be accomplished through a thorcotomy, laparotomy or laparoscopically, depending on the size of the defect and the amount of herniated tissue. The sternotomy approach has not been used to repair these hernias due to the difficult access, however if the patient requires the concomitant cardiac or anterior mediastinal procedures, the surgery can be performed adequately through a sternotomy. Use of a double lumen endotracheal tube and an internal mammary retractor greatly enhances the approach to the defect, minimally invasive cardiac surgery instruments maybe invaluable in deep chest cavities.

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Case Report

Successful Primary Arterial Switch Operation in an Adolescent

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Key Words: Transposition of great arteries, Intact ventricular septum, Left ventricular outflow tract obstruction, Primary arterial switch, Adolescent

Chettinad Health City Medical Journal 2015; 4(1): 48 - 50

Introduction

Transposition of great vessel (TGA) is a common and lethal congenital heart disease. Only 10% of the children survive beyond infancy without any intervention^{1,2}. Primary arterial switch is the procedure of choice for TGA and this procedure ideally should be done within 3 weeks of life³. Recent studies have shown that this procedure can be done up to eight weeks of life without much increase in mortality^{4,5}. TGA when associated with left ventricular outflow tract obstruction (stenosis of the pulmonary outflow) along with VSD, the life expectancy increased² as it helps in maintaining the left ventricle prepared both in terms of volume and pressure. We are reporting a case of dextro TGA with intact interventricular septum with a fibrocalcific bar which kept the ventricle prepared to enable us to perform primary arterial switch operation at sixteen years of age.

Case report

A sixteen year old adolescent female admitted with cyanosis and exercise intolerance. There was history of cyanosis since 7 month of age and she was diagnosed to be a case of transposition of great arteries at that time but not undergone any surgical procedure due to financial reasons. There was no developmental delay. There was a past history of brain abscess which was treated by external ventricular drainage. Since then the patient was on rifampicin prophylaxis and anticonvulsants. On examination the patient was thin built, cyanosed and grade 3 clubbing was noted. Oxygen saturation was 60% in room air. Clinically there was an ejection systolic murmur noted on left parasternal area. There were no features suggestive of congestive heart failure. Routine blood tests were done which showed polycythemia. Echocardiography with colour Doppler study was done which revealed. Transposition of great arteries with intact interventricular septum with severe subvalvar pulmonary stenosis (fig 1). PFO was there with bidirectional shunting and LV was found to be severely hypertrophied with mild dysfunction. Right ventricular function was normal. Cardiac catheterization revealed LV pressure of 140 mm Hg versus PA pressure of 30 mm Hg and aortic/ RV pressure of 110 mm Hg. So, LV pressure was well maintained and the left ventricle regression has been prevented by the presence of congenital left ventricular outflow tract obstruction (fig 2). So, primary arterial switch operation was planned. The child underwent arterial switch procedure with resection

of the subpulmonary obstruction. The procedure was uneventful with no significant bleeding. The fibrocalcific ring was excised and found not to be attached to the mitral valve apparatus. There was aorta-neoaorta discrepancy which was suitably tailored. ACE inhibitors were commenced for mild-moderate aortic regurgitation. She had left pleural effusion which was managed with diuresis and tube thoracostomy. Ventilation time was 22 hours and she was extubated successfully. Post operative echocardiography was showing mild subaortic stenosis with mild+ AR with mild PR and PS. On follow up after six month the patient was NYHA I. Cardiac catheterization study was done after six month of operation showing pressure in aorta was 115/51 mm of Hg, in LV the pressure was 105/25 mm of Hg and in RV the pressure was 68/12 mm of Hg. PA angiogram was showing dilated branch PA's without any PS. LV angiogram was showing mild LV dysfunction, LVH, mild MR. Parents have been counseled about the possibility of late aortic valve replacement.

Discussion

Transposition of the great arteries (TGA) is a lethal and relatively frequent malformation, accounting for 5% to 7% of all congenital cardiac malformations¹. Without treatment 28.7% infant die within first week, 51.6% infant die within first month & 89.3% infant die within first year of life².

Nearly half of the hearts with TGA have no other anomaly except a persistent patent foramen ovale or a PDA. VSD is commonly associated in 40% of the cases and a combination of VSD with LVOTO seen in about 10% cases. TGA with isolated LVOTO with intact ventricular septum is rare, seen only in 5% of cases¹. The mortality varies according to the associated defects. Patients with TGA with LVOTO and VSD have a better life expectancy than other children with TGA².

In TGA with IVS, a dynamic type of LVOT obstruction commonly seen due to dynamic leftward bulging of the basal muscular ventricular septum towards left ventricle. Fixed anatomical obstruction can be classified depending on the level and cause of obstruction. It could be valvar or subvalvar level. Subvalvar obstruction can be due to accessory mitral tissue, hypertrophied muscle bundle either discreet or funnel like obstruction, some times the tricuspid valve can

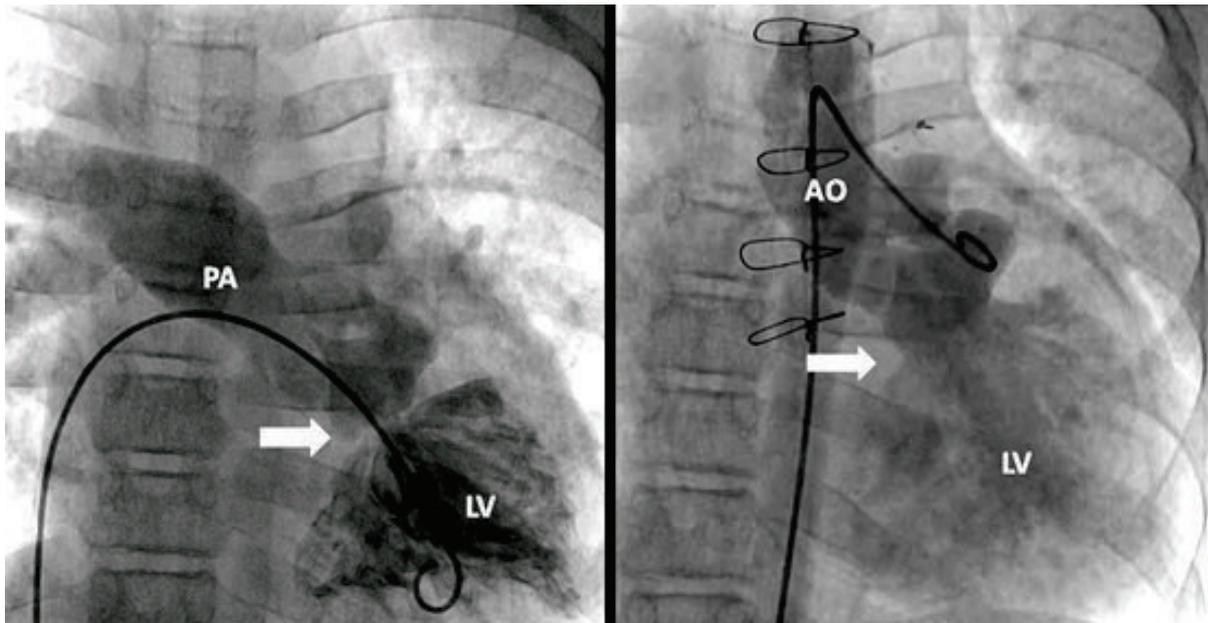


Fig 1 - Preoperative Left Ventricular Angiography (Left) showing severe left ventricular outflow obstruction and severely hypertrophied left ventricle . Postoperative Left Ventricular Angiography (Right) showing wide open Left Ventricular outflow tract.

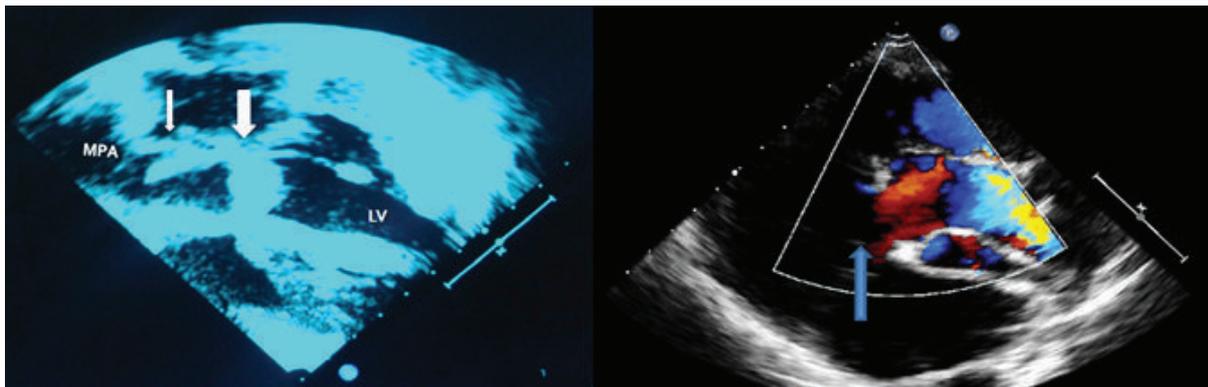


Fig 2 - Preoperative echocardiography (above) showing severe subvalvar left ventricular outflow obstruction (thick arrow) and severely hypertrophied left ventricle . Pulmonary valve is denoted by the thin arrow. Postoperative Echocardiography (below) showing wide open Left Ventricular outflow tract with neo-aortic regurgitation (blue arrow).

be prolapsed through the blocking the VSD and causing LVOTO. Obstruction can be at the valve level due to thickened and dysplastic valve or a valve with narrow annulus. Arterial switch operation is the procedure of choice for TGA as it restores the normal ventricular great artery relationship. A critical challenge of anatomic repair concerns the functional adequacy of the left ventricle which preoperatively faces the pulmonary circulation and postoperatively must handle the systemic load. In terms of early survival and postoperative primary LV failure, there is sufficient level II evidence indicating that the primary ASO may be performed in infants three to eight weeks of age with comparable outcomes to neonates. The duration of postoperative ventilation and length of postoperative hospital stay is, however, prolonged in the late ASO group⁴. Kang et al. investigated 275 neonates (younger than 21 days) and 105 infants (age range 21–185 days) undergoing the primary ASO for TGA-IVS. They found no significant difference in terms of in-hospital mortality (5.5% vs. 3.8%) or need for mechanical left ventricular (LV) support (3.6% vs. 5.7%) between the younger and older groups, respectively⁵.

According to Edwin et al. age limit for primary arterial switch operation can be extended upto 10 weeks⁶. Most clinicians however rely on the position of the septum to determine if the left ventricle is prepared enough to handle the systemic circulation postoperatively. There are many factors other than just the time duration which determines the rate regression of LV and its preparedness.

Empiric criteria for adequate LV preparation includes an absolute LV systolic pressure that is appropriate for age, RV: LV pressure ratio >0.7 , LV muscle mass within normal range for body surface area¹. Presence of LVOT obstruction is one of the factor which can help in LV preparation. In our patient subpulmonic fibrocalcific ring which prevented regression of LV and helped to maintain the LV pressure. Preoperative echocardiography showed that the subpulmonic ridge is free from mitral valve. Postoperative period was uneventful other than the early neo-aortic regurgitation which has been stable at 6 months follow up. The cardiac catheterization was done 6 months after operation showing mild LV dysfunction with normal LV pressure.

This will have to be followed up as the patient may require aortic valve replacement later with possible replacement of ascending aorta as well.

Conclusion

To summarize, Arterial switch can be attempted directly if the left ventricle regression has been prevented by the presence of LVOT obstruction. This case was an extreme example of a 16 year old presenting for a first time procedure. Review of literature mentions retraining of left ventricular function with pulmonary artery band; there is no mention of such a late primary arterial switch. Consideration for an elective annuloplasty of the neo aortic root should be given at the time of arterial switch, especially when done late to possibly prevent the development and progression of neo aortic regurgitation.

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திறுக்குறள் 941

மிகினும் குறையினும் நோய்செய்யும் நூலோர்
வளிமுதலா எண்ணிய மூன்று

மு.வ. உரை:

வாதம் பித்தம் சிலேத்துமம் என்று மருத்துவ நூலோர் கணித்துள்ள மூன்றில் ஒன்று அளவுக்கு அதிகமானாலும் குறைந்தாலும் நோய் உண்டாகும்.

Couplet 941

The learned books count three, with wind as first; of these, As any one prevail,
or fail; 'twill cause disease.

Explanation

If excessive or deficient, the three things enumerated by (medical) writers, flatulence,
biliousness, and phlegm, will cause (one) disease.

Case Report

A Rare case of LA Membrane

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Abstract

Cor triatriatum sinister is a very rare congenital heart disease, characterized by a division of left atrium into two chambers by a fibromuscular membrane. Usually it presents in early childhood. They may present with features of mitral stenosis or remain asymptomatic until adulthood.

Key Words: Cor Triatriatum, LA membrane, LV inflow obstruction

Chettinad Health City Medical Journal 2015; 4(1): 51 - 52

Introduction

Cor triatriatum sinister is a very rare congenital heart disease, characterized by a division of left atrium into two chambers.

Case report

Mrs. R 50 years old post menopausal woman is a known case of Systemic Hypertension (recently diagnosed) on regular medication. Patient had complaints of dyspnea on Exertion Class II. There were few episodes of PND. No H/O Orthopnea. She was evaluated. Her chest X-ray showed features of grade II pulmonary venous hypertension. Transthoracic Echo showed a membrane seen in LA, dividing it into proximal and distal chamber (Medial side the attachment is distal to the site of Fossa Ovalis), normal LV function, no RWMA (fig 1). Subsequently She underwent TEE which revealed thick membrane seen extending from the region of fossa ovalis to the atrial wall dividing LA into two chambers. There is a small defect in the membrane through which both the chambers are communicating (fig 2 & 3). She underwent coronary angiogram which did not show significant stenosis. Subsequently she underwent surgical resection of LA membrane.

Discussion

Cor triatriatum accounts for 0.1-0.4% of congenital heart defects^{1,2}. It is characterized by presence of an abnormal membrane dividing the left atrium into a superior and inferior chamber. The superior chamber receives pulmonary veins and inferior chamber contains the mitral valve³. The two chambers communicate through a small opening in the membrane^{1,2}. Symptoms usually occur in childhood, predominantly leads to left heart obstruction or arrhythmia.

The classification proposed by Loeffler is based on the number and size of opening in the membrane⁴. Group 1 has no opening, Group 2 has one or more opening and Group 3 has one large opening.

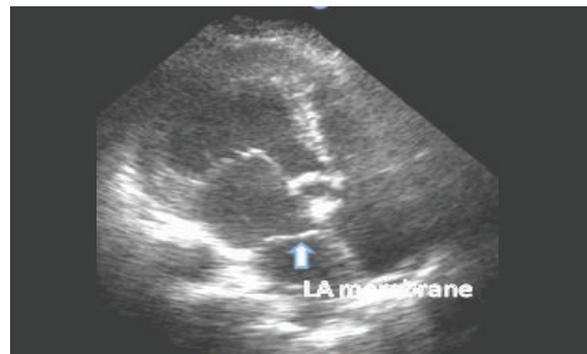


Fig 1 - Trans Thoracic Echo- Modified long axis view



Fig 2 - Trans Thoracic Echo- Modified long axis view

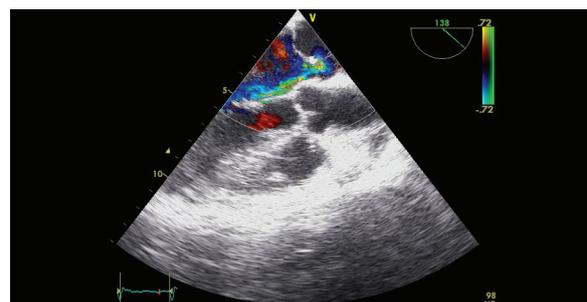


Fig 3 - Trans Thoracic Echo- Modified long axis view

The embryologic origin of this defect is unclear and may be due to defective incorporation of common pulmonary vein to left atrium^{1,5} or an abnormal septum primum 1 or a persistent left superior vena cava.

Surgery is indicated if the patient is symptomatic^{1,5}. Percutaneous balloon dilation has been done successfully in few centres¹.

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திருக்குறள் 942

மருந்தென வேண்டாவாம் யாக்கைக் கருந்திய
தற்றது போற்றி உணின்

மு.வ. உரை:

உண்ட உணவு செரிப்பதற்கான கால இடைவெளி தந்து உணவு அருந்துகிறவர்களின்
உடலுக்கு வேறு மருந்தே தேவையில்லை

Couplet 942

No need of medicine to heal your body's pain, if, what you ate before digested well, you eat again.

Explanation

No medicine is necessary for him who eats after assuring (himself) that what he has (already) eaten has been digested

Case Report

Synchronous Bilateral Non-Seminomatous Mixed Germ Cell Tumours of Testis

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Abstract

Synchronous testicular germ cell tumors with discordant histopathology are an uncommon entity. We describe a case in a 39-year-old male who presented with bilateral testicular swelling. Investigations revealed raised tumor markers and bilateral testicular lesions on scrotal Ultra Sound. Histopathology of bilateral orchidectomy showed a right testicular mixed germ cell non-seminomatous tumour comprising of immature teratoma and yolk sac (endodermal sinus) elements and a left testicular of mixed germ cell non-seminomatous tumour comprising of embryonal carcinoma and choriocarcinoma elements. This case is being presented for its rarity and unusual combination of germ cell histological tumours.

Key Words: Germ cell tumour, Synchronous, Immature teratoma, Yolk sac tumour, Embryonal carcinoma, Choriocarcinoma

Chettinad Health City Medical Journal 2015; 4(1): 53 - 54

Introduction

Among the testicular germ cell tumours, bilateral testicular germ cell tumours are a rare entity (0.5% to 5% of the testicular germ cell tumours). Within the bilateral testicular germ cell tumours, about 35% of subjects have synchronous tumours whereas 65% have metachronous tumours^{1,2}. Synchronous testicular tumours have a less favourable outcome compared to metachronous testicular tumours. It has also been found that discordant histology (that is two different histological germ cell tumours) was less commonly seen in synchronous germ cell tumours as compared to metachronous germ cell tumours¹. We report a patient with bilateral non-seminomatous tumour with discordant histology in a 39 year old South Indian male. This case is being presented for its rarity and unusual combination of germ cell histological tumours.

Case history

A 39 year old male presented with bilateral progressively increasing painless scrotal swelling. Systemic examination revealed no other organomegaly or lymphadenopathy. Investigations revealed elevated serum tumour markers; α -fetoprotein of 2332ng/ml, β -HCG of 9663.5 mIU/ml and a LDH of 395U/L. Scrotal USG revealed multiple nodular and cystic lesions in both testis. Bilateral orchidectomy was performed.

On gross pathological examination, the right testis weighed 257 grams and measured 10 x 9 x 6 cms. Cut section showed a multiple cysts with interspersed grey white firm and glistening areas (Figure 1). Microscopy revealed a neoplasm composed of glands lined by

respiratory, gastro-intestinal epithelium surrounded by primitive loose spindle (mesenchymal) cells with islands of mature cartilage. Few primitive epithelial islands were seen. Also seen were intermingling trabeculae of medium cells with moderate atypia arranged in a reticular pattern with presence of Schiller-Duval bodies (Figure 2). A diagnosis of mixed germ cell non-seminomatous tumour comprising of immature teratoma and yolk sac (endodermal sinus) elements was made.



Fig 1: Gross examination of the right testis showing partly cystic and partly solid areas.

The left testis weighed 149 grams and measured 9 x 6 x 3 cms. Cut section showed a grey white tissue with central necrosis and haemorrhage (Figure 3). Microscopy revealed extensive necrosis and haemorrhage with high grade neoplasm composed of large round cells with enlarged hyper-chromatic nuclei and prominent nucleoli, increased mitosis arranged in sheets,

solid nests. Foci of very bizarre multinucleated giant cells resembling syncytiotrophoblasts were also seen (Figure 4). A diagnosis of mixed germ cell non-seminomatous tumour comprising of embryonal carcinoma and choriocarcinoma elements was made.

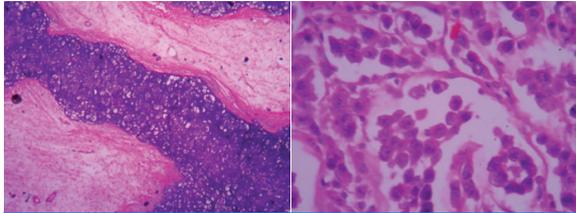


Fig 2: Photograph showing (A) mature cartilage and mesenchymal elements (Hematoxylin and Eosin, 10X) (B) organoid pattern of tumour cells with Schiller-Duval Body (Haematoxylin and Eosin, 40X)

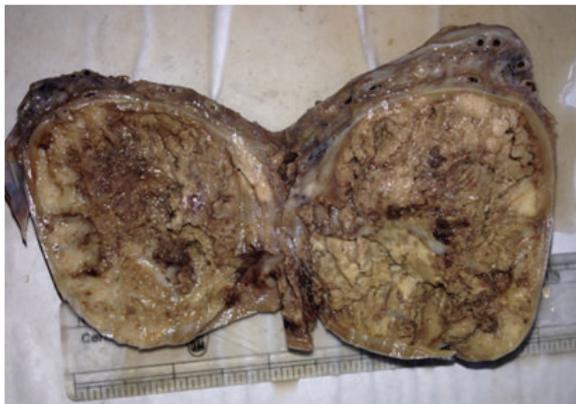


Fig 3: Gross examination of the left testis showing friable grey white tissue with necrotic and haemorrhagic areas.

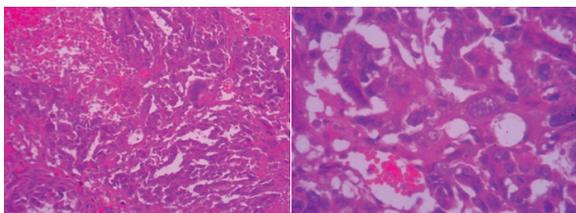


Fig 4: Photograph showing (A) bizarre multi-nucleated giant cells interspersed in a background of high grade neoplasm along with necrosis and haemorrhage (Haematoxylin and Eosin, 10X) (B) neoplastic large cells with prominent nucleoli (Haematoxylin and Eosin, 40X)

Discussion

Testicular germ cell tumours are the most common type of primary testicular malignancy¹. Among the testicular tumours, bilateral tumours including both synchronous and metachronous testicular tumours constitute 0.5 to 5% of all testicular malignancies^{1,3}. In general, men with synchronous testicular tumours were older in age at diagnosis when compared to men with metachronous testicular tumours. Also, discordant histology in the synchronous tumours was less common when compared to metachronous tumours. Men with synchronous tumour generally present at an advanced clinical stage and have a less favourable outcome as compared to men with metachronous testicular tumours^{1,2}. Current guidelines contain little information related to the management of bilateral germ cell

tumour. In general, Stage 1 mixed germ cell tumours are managed surgically with orchidectomy and post orchidectomy surveillance. If the patient cannot comply with surveillance or has high risk features like lymphovascular invasion, adjuvant chemotherapy (bleomycin + etoposide + cisplatin) is initiated⁴. However, since testicular cancer mainly affects men in their third or fourth decade of life, management must be tailored taking individual circumstances like family planning and patient preferences into account⁵.

Although bilateral synchronous testicular tumours are characterized mostly by the presence of seminomatous histology, our reported case was a rare occurrence of bilateral non-seminomatous testicular tumour. To our knowledge, very few non-seminomatous bilateral mixed germ cell testicular tumours have been reported in literature. It is important to differentiate all the histological types present in the mixed germ cell tumour to help in prognostication and also monitoring the disease. The presence of embryonal carcinoma has a bad prognosis since there is a high chance of distant metastasis^{1,6}. Elevated levels of serum alpha-fetoprotein (AFP) are seen in germ cell tumours with yolk sac component whereas elevated levels of serum human chorionic gonadotrophin (HCG) are seen in germ cell tumours with choriocarcinoma component^{1,3,6}. Our subject who had completed his family, post orchidectomy was counselled and advised chemotherapy as the treatment of choice. However, the subject refused to undergo any further management and is lost to follow up.

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Case Report

Alveolar Cysts of the Newborn with Differential Diagnosis

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Abstract

A broad range of developmental anomalies and morphological variants may occur in the oral cavity of the newborns. Dental lamina cysts, also known as gingival cysts of the newborn, are benign oral mucosal lesions of transient nature present at birth. Although the prevalence is high, they are rarely seen because of the transient nature of the lesions. They are self limiting and disappear spontaneously a few weeks or months after birth. Hence no treatment is required for such cases. Clinical diagnosis of these conditions are important in order to avoid unnecessary therapeutic procedure.

Key Words: Alveolar cyst, Gingival cyst, Newborn cysts, Bohn's nodules, Epstein's pearls.

Chettinad Health City Medical Journal 2015; 4(1): 55 - 57

Introduction

Congenital cysts are those that are present at birth. A number of complications can be associated with congenital pathologies in the oral cavity like pain on sucking, refusal to feed, respiratory difficulty because of airway obstruction, aspiration of fluids or teeth when natal or neonatal teeth are present which in turn provokes a greater stress and fear to the parents regarding these congenital oral lesions. Henirich Bohn and Alois Epstein were the first authors to describe the small palatal cysts of the fetus and newborns in 1800's¹. Thus "Epstein's Pearls" and "Bohn's nodules" were named after them. Based on the histological origin and location in the oral cavity, Fromm et al, (1967)¹ classified oral mucosal cysts as Epstein's pearls, Bohn's nodules, dental lamina cyst or alveolar cyst of the newborn. Epstein's pearls are keratin filled. Cysts that occur in mid palatine raphe region near the mucosal surface. They are believed to arise from the trapped embryological epithelial remnants present along the line of fusion of the palatal halves. Bohn's nodules are also keratin filled cysts but scattered over the palate, most numerous along the junction of the hard and the soft palate and apparently derived from palatal salivary gland structure. Dental lamina cysts are found on the alveolar ridge of the newborn or very young infants representing cysts originating from the remnants of the dental lamina. It is important that the clinician does not mistake these cysts for natal/neonatal teeth or any other pathology in the newborn and render treatment to the patient as these are transient in nature and disappear within two weeks to five months after birth². Based on the location, these cysts can be called as Palatine cysts and Alveolar cysts. Those that are located in the midpalatine raphe are called Palatine cysts and those located on the buccal, lingual or crest of the alveolar ridge are called Alveolar cysts³. The reported-prevalence of alveolar cysts in newborn ranges from 25-53%, while for palatal ones is about 65%⁴.

Case report

Consultant in oral medicine, diagnosis and radiology department was on call for a consultation in the Neonatal ICU to attend a just born male neonate born with multiple swellings in the oral cavity. History revealed that it was a full term, normal delivery of a male neonate weighing 2.415kg and length measuring 44cms with a heart rate of 130 beats / min with no complications during pregnancy or delivery. All the required vaccinations were started soon after birth and his medical history was non-contributory. The complaint was that the neonate was refrained from breast feeding due to the reasoning of intraoral swellings. General examination was unremarkable. Intraoral examination revealed the presence of two cystic swellings, one on the left posterior maxillary alveolar ridge (Fig 1) and the other on the anterior mandibular alveolar ridges (Fig 2) exactly on the midline each measuring about 3x5mm and 5x6mm in size respectively. They were roughly oval in shape with a translucent smooth shiny surface



Fig 1: Alveolar cysts on the left maxillary posterior and anterior mandible.

and well defined borders. The cystic swellings were filled with clear fluid. On palpation the swellings were soft in consistency, non-tender (as the intensity of cry did not increase with palpation of the swelling), fluctuant, compressible but not reducible. The swelling in the mandibular midline was easily displaced to the lingual sulcus and was prominent only when pushed with the tongue while the baby cry for feed. Correlating the history of swellings present at birth, their site and the translucent fluid filled nature, a provisional diagnosis of gingival cysts of the newborn was given. Considering the inconspicuous nature of dental lamina cysts, the mother was reassured and advised to proceed with normal breast feeding for the neonate.



Fig 2: Closer view of the cyst on anterior mandible

Differential Diagnosis

Eruption cyst: These are commonly seen within the mucosa overlying the teeth that are about to erupt. The cyst appears as a bluish, translucent, elevated, compressible, dome-shaped lesion of the alveolar ridge, and is one of the local disturbances to eruption of teeth. But eruption cysts are uncommon in neonates and if present are usually associated with natal or neonatal teeth and in the current presentation there was no sign of neonatal or natal teeth eruption.

Alveolar lymphangioma: These are blue, dome shaped, fluid filled lesions in the alveolar ridge present at birth and are typically bilateral but in the current presentation the two cystic swellings were single in each arch.

Congenital hemangioma: Not uncommon at birth but the site and colour of the swellings in our case does not correlate with congenital hemangioma. And there was no other red macules (portwine stain) present in current presentation.

Congenital Mucocele: Is not common and moreover in the current presentation the translucent swellings were on the alveolar ridges which are deprived of minor salivary glands.

Discussion:

Gingival cyst of newborn also known as dental lamina cyst is a true cyst. The cyst may be solitary or many in

numbers. The Gingival cysts are commonly seen in the anterior part of the alveolar ridge. In the study reported by Donley and Nelson, the cysts were more commonly seen in the maxillary arch than in the mandibular arch and whenever they existed in mandible, they also appeared in the maxilla⁵. During the bell stage of the tooth development, the dental lamina disintegrates into discrete islands of epithelial cells. Usually these clusters degenerate and resorb. Sometimes, they persist as epithelial pearls in the gingiva, or islands within the jaw, in which case they are termed as the "rests of Serres". These remnants proliferate to form small keratinised cyst. It is believed that fragments of dental lamina that remain within the alveolar ridge mucosa after tooth formation proliferate to form these small, keratinized cysts⁶. The majority of these cysts degenerate and involute or rupture into the oral cavity within two weeks to five months of postnatal life^{7,8}. They are generally asymptomatic and do not produce any discomfort for the infant. Most authors do not recommend any treatment since the lesions are asymptomatic and disappear spontaneously by fusing with the oral epithelium and discharging its contents into the oral cavity during the neonatal period^{5,6,7}. In accordance with Donley's study the current presentation also proves that mandibular cysts are usually accompanied by maxillary cysts and the literature review shows that most of the newborn cysts reported were single in number in contradiction to this presentation of two cysts each one in the maxilla and mandible⁵.

Conclusion

It might be jittering for the parents to see a swelling in the newborn but as dental lamina cysts are benign, asymptomatic and transient, reassurance to the parents regarding the benign and self healing nature of the swelling is the best recommended advice. A close follow up of the condition is mandatory to confirm the clinical diagnosis as in cases similar to ours where the baby is just born and no invasive investigatory procedures could be performed. In the current presentation the neonate was reviewed after a week during which there was remarkable decrease in the size of the cysts.

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Enigma of HIV 'Cure'

The Second Case of Apparent HIV "Cure" in a Baby from Milan, Italy following the case of the "Mississippi baby" that received widespread attention in 2013/2014 raised many questions about the immune dynamics of any viral infection¹.

The Lancet reported a case from University of Milan, of a baby born to a HIV-positive mother, who was 'transiently cured' of HIV following ART treatment, but to later exhibit detectable HIV infection. The baby was born in December 2009, intensive ART treatment instituted shortly after birth and appeared to have been cured of HIV in 3 years time. The viral load indicated that the virus had been eradicated and even antibodies to HIV disappeared to become seronegative. This indicated that the immune system has overcome the infection and even the virus disappeared from the system so that no more antibodies need to be produced to curtail the virus. The ART was stopped with the mother's consent and the child remained negative for two years, to show up HIV viral load again. The researchers concluded that the viral reservoirs had not been eliminated by ART, despite the virus being undetectable for more than 2 years, but kept at bay. Though the authors suggest that the child's high viral load at birth, infection in utero and low birth weight, may have precluded long-lasting viral remission, the virus stayed in the system and the original infecting strain rebound². The antiretroviral drugs though have substantially decreased HIV morbidity and mortality in the world, these drugs may not eradicate the virus and eliminate viral reservoirs in toto. This may not be necessary in the context that many of these epidemics are 'attenuated' in the long run, and such rebound from reservoirs in spite of the protective immunity induced are known in many diseases. Understanding the mechanism of this remission and relapse thus is a priori in infectious diseases research.

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- Dr. Pitchappan

Case Report

Unusual Ocular Manifestations in a Patient with Alport's Syndrome

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Key Words: Alport's syndrome, Coloboma, Thin basement membrane disease

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Introduction

Alport's syndrome or hereditary nephritis is a rare genetic disorder of basement membrane, clinically characterized by haematuric nephritis, sensorineural deafness and characteristic ocular manifestations¹. We report a case of Alport's syndrome with unusual ocular presentation featuring bilateral congenital coloboma of optic disc with unilateral pigmentary retinopathy. This is a rare ophthalmological finding in Alport's syndrome.

Case summary

A 23 year old male presented with bilateral progressive diminution of vision for one year and progressive hearing loss for 6 months. Patient also had decreased urine output and swelling of both legs for the 2 months, shortness of breath and easy fatigability for one month. Patient gave a history of renal calculi since 15 years, which had been managed conservatively. There was a history of kidney disease in both of his brothers. His elder brother had macroscopic haematuria and proteinuria while the other had renal calculi. Both of them did not have renal dysfunction severe enough to need active intervention.

On examination, patient had pallor with bilateral pedal edema and hypertension (BP160/100 mmHg). Respiratory examination revealed bilateral basal crepitations and other systems were normal. His visual

acuity was diminished. Slit lamp examination of eyes revealed bilateral congenital coloboma of optic disc with unilateral pigmentary retinopathy in the left eye (Fig 1).

His Hb was 4.8 gm/dl with total WBC count 9700/mm³, blood urea was increased (133 mg/dl), the serum creatinine was elevated (35.30 mg/dl), and his electrolytes were normal. Urine examination showed proteinuria (albumin 3+) and microscopic haematuria. Renal ultrasound showed bilateral contracted kidneys (left- 5.8 x 2.8 cms, right- 6.2 x 2.8 cms) with loss of corticomedullary differentiation. Audiometry revealed bilateral moderate sensorineural hearing loss.

As patient was very apprehensive about renal biopsy and he had bilateral contracted kidneys, renal biopsy was deferred.

On the basis of typical triad of positive family history, sensorineural deafness and medical renal disease, a clinical diagnosis of Alport's syndrome was made. Patient was treated with diuretics, antihypertensives, blood transfusion, hearing aid and maintenance hemodialysis.

Discussion

Alport Syndrome is a progressive form of thin basement membrane disorder with an approximate incidence of 1 in 50,000 live births². It is a disorder arising from mutations

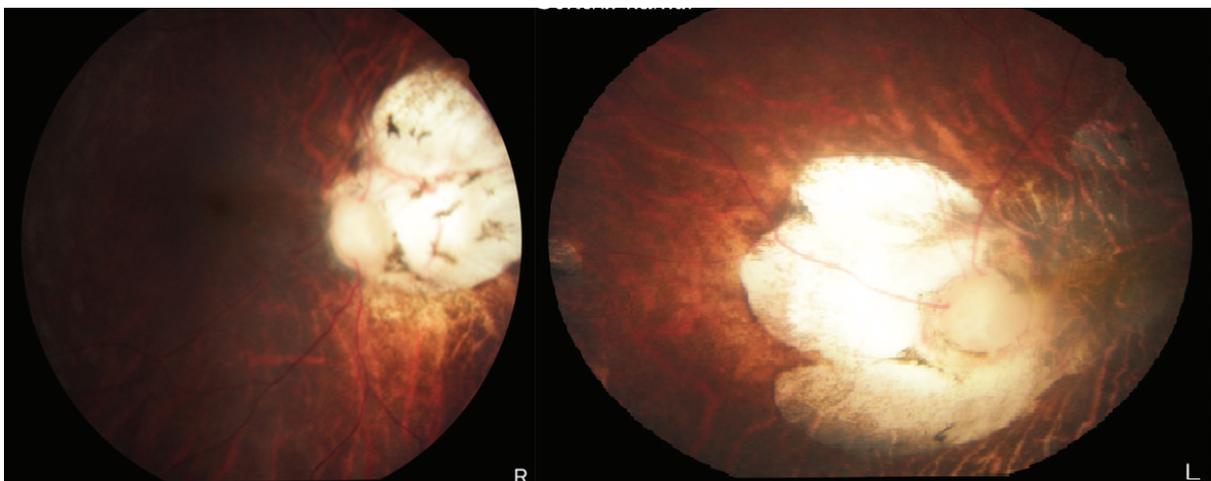


Fig 1 - Slit-examination showing bilateral congenital coloboma of optic disc, left eye unilateral pigmentary retinopathy

in type IV collagen (*col4A3*, *col4A4*, and *col4A5*) biosynthesis genes³. It develops at a younger age and occurs more common in males due to X linked dominant inheritance pattern. Thus, an impairment or change in collagen network found in the glomerular basement membrane, cochlea and anterior lens capsule will lead to gross or microscopic hematuria, proteinuria, end stage renal disease, bilateral sensorineural hearing loss and ocular defects like anterior lenticonus (commonest), posterior capsular cataract, capsular dystrophy, Dot and Fleck Retinopathy⁴. The other rare ocular manifestations include posterior polymorphous corneal dystrophy, posterior lenticonus, cataract, recurrent corneal erosion and macular degeneration⁵.

Our patient had bilateral congenital coloboma of optic disc, causing impairment of visual fields, along with dot and fleck retinopathy.

Even though diagnosis of Alport's Syndrome can be made by the classical triad, electron microscopic examination of renal biopsy specimen is diagnostic in cases without classic findings. But in our case, since biopsy was not done, the differential diagnosis included were other glomerular disorders that are present with microscopic hematuria like IgA nephropathy and thin basement membrane nephropathy. In IgA nephropathy, family history is usually negative and in thin basement membrane nephropathy, the family history may be positive for hematuria, but renal failure and deafness are typically absent.

Treatment involves conservative medical management, dialysis or renal transplantation for renal failure. If ocular manifestations like anterior lenticonus and posterior capsular cataract cause visual impairment, they can be managed by lens extraction. Hearing aids are useful in those with sensorineural hearing loss.

Conclusion

The characteristic clinical manifestations of Alport's syndrome are hematuric nephritis, hearing and visual defects. However, the presence of other ocular defects such as coloboma should also prompt a search for Alport's syndrome.

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Case Report

Surgery for Far Lateral Disc Prolapse

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Abstract

Far lateral disc prolapse offers a diagnostic and management challenge. Patient clinically present with radiculopathy of the exiting nerve root at that level. These are being increasingly diagnosed after the advent of Computed tomography (CT) and Magnetic resonance imaging (MRI). Surgical approach is different from the regular approach to the lumbar disc. This case report highlights the clinical presentation and the use of inter transverse muscle splitting approach for far lateral disc prolapse.

Key Words: Far lateral disc, Extra-foraminal approach.

Chettinad Health City Medical Journal 2015; 4(1): 60 - 62

Introduction

The term far lateral disc prolapse is applied to disc protrusion occurring outside the intervertebral foramen and it compresses the nerve root exiting at the same level in contrast to the normal posterolateral disc prolapse which compresses only the traversing root. Failure to identify this may lead to wrong diagnosis, management and persistence of pain after surgery. Incidence of far lateral disc is about 7-12% of all disc herniations¹. Since far lateral disc compresses the exiting nerve root, the clinical presentation corresponds to the radiculopathy of exiting nerve root in contrast to the regular posterolateral disc protrusion and is being increasingly diagnosed after the advent of Computed tomography (CT) and Magnetic resonance imaging (MRI). Surgical options for a far lateral disc is different from normal posterolateral disc protrusions. In this report a case of far lateral disc protrusion at L4-L5 level is presented with emphasised clinical presentation and use of inter transverse muscle splitting approach.

Case report

A 41 year old man presented with low back pain which is radiating to the left lower limb through the back of the thigh upto the front of the leg corresponding to the L4 root distribution since 3 years with aggravation of pain on walking and numbness in the lower part of the leg. Neurologic examination shows weakness of knee extension and dorsiflexion of the foot on the left side, with the impairment of sensation over the L4 dermatome on the left side, straight leg raising was positive at 60 degrees on the left side. MRI of lumbosacral spine showed evidence of far lateral extraforaminal disc prolapse at L4-L5 (Fig 1). Patient was taken up for surgery for far lateral disc prolapsed by inter transverse muscle splitting approach.

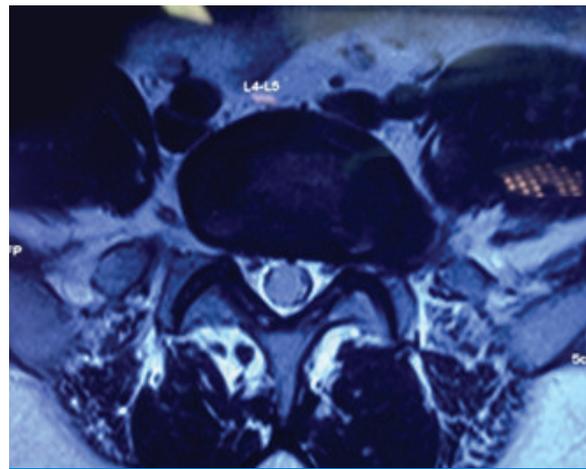


Fig 1 - MRI - LS Spine Showing Left Far Lateral Disc

Surgical Technique

Under general anaesthesia, patient was placed in prone position. Inter transverse space between L4-L5 was identified with c-arm. Paramedian skin incision was made (5cm away from the midline). Inter transverse space was approached after splitting the muscles (multifidus and longissimus), transverse process was identified by palpation. Level was reconfirmed with c-arm. Under operating microscope, the posterior primary ramus and the spinal nerve was identified, where it passes through the medial aspect of the inter transverse ligament and soft tissues were dissected carefully, preserving the nerve root. Lateral aspect of the superior articular process of the facet was drilled using diamond burr, nerve root was identified and separated and disc protrusion under the nerve root was seen, which was removed using disc punch (Fig 2) and nerve root was decompressed and remaining degenerated disc material was cleared from the space.

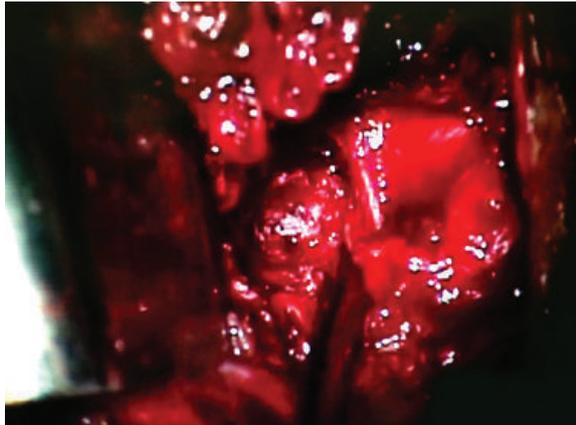


Fig 2 - Showing Intraoperative Far Lateral Disc

Post operatively patient had complete relief of radicular pain, motor and sensory deficits started improving. Patient is doing well at the end of 1 month follow-up without any residual discomfort (Fig 3).



Fig 3 - Postoperative Scar

Discussion

Far lateral disc refers to herniation of the disc at or lateral to the intervertebral foramen. This position usually compresses the exiting nerve root at that level for example, far lateral disc protrusion at L4-L5 compresses L4 root in that side and L5-S1 compresses L5 root in that side. This is in contrast to the usual posterolateral disc protrusion which presents with radiculopathy of the nerve root leaving below the level.

Far lateral disc prolapse was first described by Lindblom in 1944 in a cadaver². Macnab et al³ and Abdullah et al⁴, described the clinical syndrome of extreme lateral disc herniation. The diagnosis of the far lateral disc remained difficult till the advent of CT and MRI era in the mid 1980's. The incidence of far lateral disc is estimated to 7- 12% of all disc herniations¹ and can be foraminal and extraforaminal components.

Various resection techniques are employed for removal of far lateral disc herniations, medial facetectomy, inter-transverse technique⁵, full facetectomy, trans-pars technique, extra-foraminal: technique (extreme lateral) approach, endoscopic techniques, anterolateral retroperitoneal approach with or without fusion and pedicle screw fixation. The extent and type of facet resection and decompression employed to approach far lateral disc herniations must be individualised, as no one technique is universally appropriate¹.

The extreme lateral extra-foraminal technique (technique followed in our department) exposed through midline or preferably paramedian muscle splitting approaches, affords access only to the far lateral compartment and nerve root^{6,7,8}. Removal of the intertransversarius ligament and fascia adequately exposes the far lateral compartment. The superolateral portion of the facet must also be removed to caudally identify the more medial portion of the far laterally exiting nerve root.

The exposure is appropriate for pathology confined to the far lateral compartment beyond the pedicles⁶. Darden et al excised 25 far lateral discs using the muscle splitting approach and obtained a 2 year follow-up; 48% exhibited excellent, 32% good, 20% fair/poor results with surgery⁹. In Siebner and Faulhauer's series of 40 patients with far lateral disc prolapse removed through 38 midline and 2 paramedian extra-foraminal approaches, pain was successfully relieved in 85% of their patients. The minimal bony decompression and facet excision limited instability⁶. Extra-foraminal technique provides excellent exposure of far lateral pathology. Limitations of the extra-foraminal technique include the inability to remove disc medially and the lack of access to foraminal and intra-canalicular spondyloarthrosis.

Inter transverse muscle splitting approach used in this patient involves no major resection of bone and spine stability is not affected. Limitations are unfamiliar anatomy and difficulty in the removal of the more medially placed disc protrusion.

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Mom's Fibre-Rich Diet Keeps Baby's Asthma Quiet

Whether an offspring develops asthma or not depends on what its mother eats during the pregnancy. That is apparently the conclusion of a study carried out at Monash University in Australia (Nature Communications, doi: 10.1038/ncomms8320, published online 23 June 2015). The study was done both in pregnant mice and pregnant women. Pregnant mice fed with high fiber diet delivered offspring that did not develop symptoms of asthma later in life in contrast to the offspring of mice fed low fiber diet. Similarly, offspring of women who consumed fiber-rich diet during their pregnancy, were less prone to develop asthma related symptoms later in childhood. Apparently, high fiber diet induces changes in gut bacterial flora leading to preponderance of those microbes that release anti-inflammatory substances. These in turn suppress asthma related genes (*Foxp3* gene) in the offspring.

- Dr. K. Ramesh Rao

From the Pages of History

History of Semen Analysis

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Semen analysis is an important tool in the diagnosis of male infertility. Through its cellular and chemical components, human semen can provide information on the functional properties of the organs producing this fluid i.e., the testis, epididymis, and accessory glands¹.

This important test has its origins traced back to 1677 when Anton Van Leeuwenhoek (Fig 1), a Dutch master craftsman, first observed human spermatozoa from an ejaculate, along with his student, Johan Ham. Using a simple microscope which he created, he observed millions of small motile 'animals', which he called animalcules (Fig 2 & 3). In his letter to the Royal Society of London, he illustrated the structure of spermatozoa quite accurately that in retrospect, his observations with the help of such a primitive microscope seem incredible². It is interesting to know that this landmark letter to the Royal Society, which paved way for modern Andrology, was written and sent in the fear of being considered repugnant and even scandalous due to the nature of the sample. Leeuwenhoek was also the first to observe the serpentine motion of the animalcules and he also observed different shapes of spermatozoa across different species³.

Almost a hundred years later, it was Lazaro Spallanzani in 1771, after extensive work on artificial insemination, observed spermatid animalcules in various species, including humans and even documented the fertilizing capacity of the sperm⁴.

While numerous spermatologists continued to work on spermatozoa characteristics during that period, it was Rudolf Wagner in 1837, who made substantial contribution by documenting his observations on spermatozoa of more than 400 species, including humans. Wagner, back in those days observed that, 'the motility of the sperm was greatest at the point of ejaculation and was less in sperm taken from vas deferens and even lesser or non-existent in sperm taken from testis'⁵.

Further highlight was placed on spermatozoa through J.Marion Sim's work on post coital cervical mucus test. He made an important observation which is significant even today, that the presence of spermatozoa indicates that the male is not barren⁶. It was a landmark paper by Macomber and Sanders in 1929 that quantitatively assessed spermatozoa. From the study which involved 294 males, it was deduced that a 'normal' reference value of above 60 million/ml significantly increases the chances of pregnancy. They also tried to establish a method for counting spermatozoa with the help of a blood counting chamber⁷.

The 'normal' values were lowered to 40 million/ml by Amelar and Williams⁸ and subsequently brought down to 20 million/ml after the remarkable study done at that time by John MacLeod on 1800 men comparing sperm characteristics between fertile and infertile populations⁹.

Further contribution to 'normal' values was done by Rune Eliasson who stated that it was not justified to discriminate a semen sample with 5million/ml sperm concentration as infertile¹.

Based on a number of studies done by the above mentioned pioneers of Andrology, the World Health Organisation(WHO) published its first manual on semen analysis in 1980¹⁰, thereby helping establish uniformity in methods of evaluating spermatozoa worldwide. It has been updated periodically with the fifth edition currently being in use¹¹. While the first few editions seem consensus- based, the fifth edition appears mostly evidence-based, despite the discrepancies and despite being limited to a select population. The introduction of CASA systems in 1990's paved way for extensive studies on sperm kinesiology and a relatively more subjective way to conduct semen analysis.

Spermatozoa Morphology: Morphology of spermatozoa requires a special mention as it has been the most debated issue in spermatology due to its heterogeneity and subjective nature of evaluation. Since 1900s studies have been conducted to equate normal morphology to sperm fertilization capacity.



Fig 1: Anton van Leeuwenhoek (1632 - 1723)



Fig 2 - Simple microscope created by Leeuwenhoek

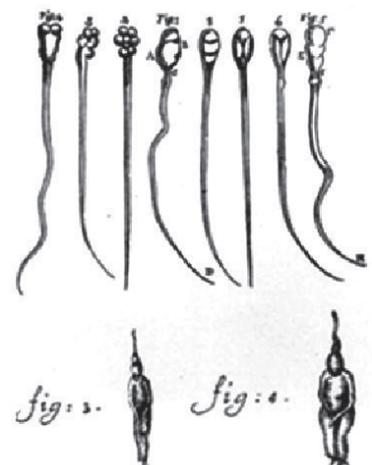


Fig 3 - Illustrations of spermatozoa by Leeuwenhoek

Interestingly, until 1970's, it was only the head of the spermatozoa that was considered while assessing morphology. It was in 1971 that Rune Eliasson emphasized the importance of evaluation of the whole spermatozoon including the mid-piece and tail. Eliasson was one of the first to standardize this parameter through a classification system containing three groups – head, mid-piece and tail¹².

Evaluation of sperm morphology has seen two approaches – liberal and strict. The liberal approach as followed by MacLeod, considered all forms to be normal except those that were highly distorted, therefore no criteria was put forth for normal spermatozoa¹³. But in the strict criteria, as described by Menkveld and Kruger, even borderline forms are to be considered abnormal. A normal spermatozoa was defined on the basis of spermatozoa obtained from the internal cervical os (after coitus) and from those tightly bound to zona pellucida¹⁴, thereby providing guidelines which were adopted by the WHO manual. The WHO manual in its first two editions followed the liberal approach after which it implemented the stricter criteria¹²; this would explain the dramatic reduction in the normal morphology reference value from 80%(1st edition)¹⁰ to 4%(5th edition)¹¹.

In spite of the strict criteria description, the subjectivity of sperm morphology assessment makes it difficult to standardize this parameter, and bring uniformity across different labs; this results in a significant inter and intra observer variability. This is beautifully described by Eliasson using Edward Adelson's checker shadow optical illusion example, as shown in fig 4^{15,16}.

Conclusion

While semen analysis is an important tool in diagnosing male infertility, it is to be remembered that reference ranges given by the WHO manual are not diagnostic cut-off values but only results obtained out of an observation of a fertile population.

Male fertility cannot be determined solely on the result of a semen analysis as there is no evidence stating the exact number and quality of sperm required for a man to be considered fertile. As Christopher De Jonge rightly said, semen analysis is still the subject of both commendation and condemnation¹⁷.

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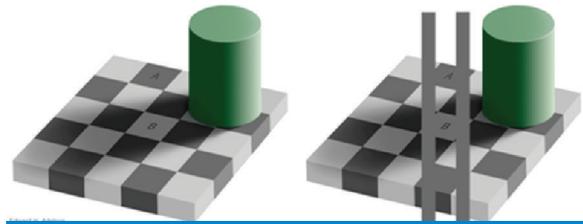


Fig 4 : Adelson's checker shadow optical illusion. In this checker - shadow image, the squares A and B have exactly the same shade of grey.

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