

# **WHAT IS THE BEST INTERVENTION FOR SEVERE CORONARY ARTERY DISEASE**

**Professor D. Taggart – John Radcliffe Hospital, Oxford.**

*A multidisciplinary approach is essential but best evidence still favours surgery over percutaneous intervention*

For the last two decades coronary artery bypass grafting (CABG) has been the ‘gold standard’ treatment for patients with severe multi-vessel ischaemic heart disease [IHD] [1]. In the last few years, however, CABG has been increasingly challenged by percutaneous coronary intervention (PCI). Indeed, in many parts of the developed world PCI is now at least twice as frequent as CABG raising several questions over this profound change in practice. Why has it occurred? Is it evidence based? Does it represent best value for money? Are patients appropriately informed of its limitations?

CABG is the most intensively studied surgical procedure ever undertaken with follow-up data extending to over twenty years [2]. It is highly effective in relieving the symptoms of IHD and improving life expectancy in certain anatomic patterns of disease; and these benefits are magnified in those with more severe disease and with impaired left ventricular function [1]. Furthermore, CABG is a remarkably safe therapy. Improvements in medical, anaesthetic and surgical management has ensured that the hospital mortality has remained around 2% over the last decade despite an ageing and sicker CABG population [3].

On the other hand and until recently PCI has traditionally been used to treat patients with one or two vessel coronary disease. Its current use in patients with more widespread disease has largely mirrored its development from simple balloon angioplasty to a procedure involving deployment of (multiple) stents. The conventional Achilles heel of simple angioplasty is re-stenosis, affecting up to 40% of procedures, and this is halved by stents. Most recently there have been several claims that drug-eluting stents can effectively eliminate re-stenosis.

So is PCI really as effective as CABG? Ten randomised trials have compared PCI and CABG in patients with ‘multi-vessel’ IHD. Overall the trials broadly agreed that there was little difference in survival with either intervention but that surgery markedly reduced the need for further intervention from 20% with PCI to 5% with CABG. However, 80% of the trial patients actually had single or double vessel disease and normal ventricular function [4], a population already known not to benefit prognostically from CABG [1]. In effect the trials were inherently biased against the prognostic

benefit of surgery in patients with severe three vessel coronary artery disease who largely constitute the population undergoing surgery in the 'real world'.

Subsequent reporting of these trials in the medical literature was disingenuous. Although styled and titled as trials of multi-vessel IHD it was only to the expert reader prepared to pursue the small print that the highly unrepresentative nature of their patient populations became apparent. Accompanying editorials, invariably written by cardiologists, either ignored or fleetingly addressed this fundamental limitation.

Despite this, these trials are now used to justify PCI in patients with true multi-vessel IHD. The danger of this approach was highlighted in a recent study from the Cleveland clinic in which propensity matched patients with severe coronary artery disease had a two and a half fold increase in five-year mortality when PCI rather than CABG was used as treatment [5]. And this belies the over-simplicity of cardiological justification for PCI that the patient 'did not want an operation'. Patients generally want what is in their best interest. To most, a week in hospital and six weeks recuperation is a good trade-off for a procedure offering an excellent prospect of long-term relief of symptoms and a gain in life expectancy.

What of the safety and economics of drug-eluting stents? In contrast to the well-established long-term outcome of CABG most studies of these stents have follow-ups of less than a year. The early promise that they 'eliminate' restenosis appears increasingly improbable as registry rates of restenosis, reflecting outcome in real practice, are reported at 10%-20% in more complex lesions [6,7] and as high as 28% in bifurcating lesions [8]. And as these stents inhibit endothelialization the patient is at subsequent risk of myocardial infarction even up to a year later if anti-platelet medication is stopped [9]. These limitations reinforce NICE's caution in 2003 that a long overdue expansion of CABG with its proven benefits is jeopardised by the widespread use of these expensive stents [10].

So in this era of evidence-based medicine how best should we advise the patient with severe multi-vessel IHD? PCI should only become the 'default' treatment when there is supportive evidence from relevant trials that PCI is really as safe and as effective as CABG. The current tendency of the cardiologist to exclusively investigate and treat patients with severe multi-vessel IHD without a surgical opinion not only belittles the traditional multi-disciplinary approach but ensures that the best and most balanced advice is unlikely to be consistently offered. Most importantly, by effectively denying the patient the opportunity of making a fully informed choice, it falls far short of best practice.

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# **UNSTABLE ANGINA: EARLY SURGICAL REVASCULARISATION**

## **FOR ALL?**

**Mr. D. Pagano – Queen Elizabeth Hospital, Birmingham.**

The role of revascularisation for patients with acute coronary syndrome without Q-wave myocardial infarction remains controversial. Acute coronary syndrome encompasses a wide range of patients, from those presenting with non-ST elevation myocardial infarction to those who have recent onset angina without evidence of myocardial necrosis. The “old” surgical trials of unstable angina [1, 2] had not identified a clear survival benefit of coronary revascularisation over medical therapy, except for patients with moderate LV dysfunction (ejection fraction between 30% and 50%). However, the limitations of these trials in which there was a 30% cross over from medical to surgical treatment and with the “best” medical treatment of the time pre-dating the introduction of statins and angiotensin converting enzyme inhibitors are well known. It has been common practice to recommend surgical revascularisation for patients with unstable angina on the basis of the same indications advocated by the trials of coronary artery bypass grafting in patients with chronic coronary artery disease.

The recent understanding of the pathophysiology of acute coronary syndrome and the advent of percutaneous revascularisation techniques led to the design of new trials of treatment of unstable angina. In these studies patients were randomised to an “early invasive” and an “initial conservative” strategy [3-6] Coronary revascularisation was achieved largely by percutaneous techniques and coronary artery bypass grafting was used in approximately 20% of patients. The main end-points of these studies were a composite of mortality, incidence of myocardial infarction, re-hospitalisation or refractory angina.

The results have been variable. The VANQWISH study demonstrated an adverse effect of the early revascularisation strategy compared with the more conservative approach, while the three more recent trials (FRISC II, TACTICS and RITA III) suggest a benefit associated with an early revascularisation strategy. These benefits consist mainly of a reduced incidence of non-fatal myocardial infarction [4, 5], recurrent or refractory angina [6] and/or re-hospitalisation [5]. No study has demonstrated a clear

survival benefit for either approach. On the basis of these findings, there is a tendency to recommend early revascularisation for patients with acute coronary syndromes who have not suffered a Q-wave myocardial infarction. This policy is supported by the fact that percutaneous revascularisation techniques have become safer and more effective, particularly with the advent of stenting and the introduction of drugs that effectively downgrade platelet activity. Can we extend these recommendations to patients who need surgical revascularisation?

The studies did not specifically analyse the results of patients who required CABG. However, in the VAMQWISH trial a high in hospital mortality (11%) was detected among patients undergoing CABG at a median of 8 days from admission (FIG). This compares unfavorably with the mortality of other trials and that of patients undergoing CABG at a median of 24 days in the same trial. These studies appear comparable for most known patient related risk factors associated with increased operative mortality and the only significant difference can be found in the degree of myocardial necrosis at time of enrollment. In VANQWISH all patients had a CK/CK-MB rise greater than 1.5 times the upper limit of the reference level of the enrolling hospital. In the FRISC II trial the prevalence of raised CK/CKMB in the patients enrolled is not reported, however in this study less than 60% of the patients had a troponin-T rise  $\geq 0.1$  g/L. In TACTICS only 37% of the patients had a CK-MB rise, but this was small ( $< 3$  times the upper reference limit for each hospital), and over 40% of patients in the study had no troponin rise [7]. In RITA III CK/CK-MB rise was an exclusion criteria for entry. All the patients in the VAMQWISH study had myocardial infarction, albeit non-Q, and the influence of timing of surgery on mortality in this group is well known. In the study by Curtis et al [8] the mortality of patients undergoing CABG within a week from MI ranged between 18.6% and 7.4% and decreased significantly to 2.7% if surgery was performed after 3 weeks. A recent study of 5517 patients undergoing CABG showed that in-hospital mortality was highest in the group undergoing surgery within 1 week from MI (13%) [9]. Finally, the mortality of patients undergoing CABG within 30-days from MI in UK in 2000 and 2001 was 5.9% and 6.3 % respectively [10]. This was significantly higher than for patients without MI (2% and 1.9% respectively) and remarkably similar to the overall mortality of the patients in VANQWISH undergoing surgical revascularisation (7.7%).

It is not possible to differentiate between non-Q and Q-wave MI in these reports, and there are

no studies to address the relationship between level of CK rise and perioperative mortality.

How do we screen patients presenting with acute coronary syndrome?

By comparison with the other trials that used Troponin (T or I) VANQWISH used ‘conventional’ cardiac enzymes as markers of myocardial damage. In that study myocardial damage was biochemically defined as: *“one or more cardiac enzymes (Creatine kinase; CK, Aspartate Amino Transferase; AST, or Lactate dehydrogenase; LDH) reaching 1.5 times above the laboratory upper limit of normal and/or two consecutive CK and Creatine kinase MB fractions (CK-MB) separated by 4 hours to exceed the upper limit of the laboratory reference interval”* [11].

These criteria for myocardial injury are not consistent with current views (ref). Troponin (I or T) measurements alone are often used for the detection of myocardial necrosis. This does not reliably differentiate between “small” and “significant” injury. Myocardial damage sufficient to release a detectable increase in conventional cardiac enzymes is usually considered MI. To detect patients who have significant myocardial damage and are at high risk of peri-operative mortality assessment of conventional myocardial enzymes in addition to Troponins is therefore essential. The standards recommended by the American College of Cardiology and by the European Society of Cardiology advise that most sensitive and specific non-Troponin biochemical marker of myocardial damage is CK-MB (mass measurement). A biochemically significant amount of myocardial injury consistent with an MI occurs when:

- CK-MB exceeds the 99<sup>th</sup> percentile of a reference control value on two successive samples.
- Or a maximal value 2 times the upper limit of normal for that laboratory on one occasion after the index clinical event.

For those laboratories that might not use CK-MB, a pragmatic approach would be the use of total CK. However, the sensitivity and specificity of this marker is lower than CK-MB and this could lead to a small but significant proportion of patients at greater operative risk.

In summary, review of the recent unstable angina trials suggests therefore a pragmatic strategy for the patients in need of surgical revascularisation. The key factor seems to be whether there has been a CK/CK-MB rise and this information should be gathered in addition to the troponins. In patients without CK rise but with abnormal troponins, these studies suggest that

the potential benefits of an early revascularisation approach are not offset by elevated operative mortality. In the patients with more pronounced myocardial necrosis waiting for at least 3 weeks, if clinically acceptable, may come with a significantly reduced operative mortality. The risk of operative death in patients with CK rise needing early surgical revascularisation remains high.

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# **SURGICAL APPROACHES FOR REVASCULARISATION:**

## **CARDIOPULMONARY BYPASS FRIEND OR FOE ?**

**Mr M. Underwood - Bristol Royal Infirmary.**

The routine use of cardiopulmonary bypass to facilitate myocardial revascularisation has been called into question in recent years with the development of 'off-pump' techniques allowing coronary artery bypass surgery to be performed on the beating heart. This lecture will review the data from retrospective analyses, randomised trials and meta-analyses surrounding this hotly debated issue. The references given below represent recent review articles which attempt to put all the available published evidence into context.

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# SURGICAL APPROACHES FOR REVASCULARISATION

## CONDUIT CHOICES AND THE EVIDENCE BEHIND THEIR USE

**Mr. G. Cooper – Northern General Hospital, Sheffield.**

Acute coronary syndrome (ACS) describes a spectrum of clinical conditions ranging from ST segment elevation to non-ST segment elevation myocardial infarction and unstable angina (ACS without enzyme marker release) whose common pathology is characterised by disruption of a vulnerable coronary artery plaque complicated by intraluminal thrombus, embolism and varying degrees of ischaemia. Despite advances in management, morbidity and mortality remain high and these patients present a considerable burden to UK healthcare resources.

Successful management depends upon accurate diagnosis and risk assessment coupled with antiplatelet (aspirin/clopidogrel), antithrombotic (low molecular weight heparin) and anti-ischaemic (β-blockers, nitrates) therapy. Patients whose risk is high, based upon clinical risk scores and marker enzyme (usually troponin) levels, benefit from more aggressive treatment with platelet glycoprotein receptor antagonists as a preamble to early in-hospital angiography with a view to revascularisation. Application of these evidence based guidelines from Europe and the USA has rapidly overwhelmed cardiological resources in the UK and over 50% of catheter laboratory time is now dedicated to the management of acute coronary syndromes with waiting times for inter-hospital transfer frequently exceeding one month.

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# **SURGICAL MANAGEMENT OF HEART FAILURE**

**Professor W. A. Baumgartner – The John Hopkins Hospital, Baltimore, U.S.A.**

Heart Transplantation is the gold standard treatment for the endstage congestive heart failure. A newer procedure (Surgical Ventricular Restoration – SVR), introduced by Dr. Vincent Dor in the late 1990's has been associated with positive clinical outcomes including survival and quality of life. The surgical technique, based upon that of Dr. Dor and Dr. Lorenzo Menicanti, uses a transition zone or the base of the papillary muscles as the area to begin the encircling anterior septal purse string suture. Another technique employed by Dr. John Conte of John Hopkins Hospital utilizes an intra-ventricular sizing device calculated to a left ventricular end-diastolic volume index of 50-60 ml/m<sup>2</sup>.

The recent RESTORE multicenter study, which evaluated outcomes following SVR in 1198 patients with congestive heart failure, found that there was both improved left ventricular function and excellent five year survival rate of 69% in this group of patients with ischemic cardiomyopathy following an anterior wall myocardial infarction.

Concomitant coronary artery bypass grafting and mitral valve repair are employed with this operation when indicated. A mitral valve procedure (repair/replacement) is recommended in all patients with moderate to severe mitral regurgitation.

Left ventricular assist device implantation is another alternative approach for the treatment of ischemic cardiomyopathy. The randomized evaluation of mechanical assistance for the treatment of congestive heart failure (REMATCH) trial demonstrated superior outcomes in patients receiving a left ventricular assist device versus those aggressively managed with medical therapy. Despite these promising results, there are still significant issues associated with mechanical assistance including durability, cost, blood/surface contact, and infection. SVR is an alternative procedure that can be performed and does not preclude subsequent heart transplantation or left ventricular assist device implantation if required.

This talk will primarily focus on the surgical ventricular restoration procedure, indications, appropriate candidates, operative technique, outcomes and future refinements. The procedure will be also contrasted with heart transplantation and left ventricular assist device implantation.

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# INDICATIONS FOR SURGERY FOR NATIVE AND PROSTHETIC

## VALVE ENDOCARDITIS

**Mr. C. Munsch – Leeds General Infirmary.**

### **Native**

- Acute AR or MR with heart failure
- Acute AR with tachycardia and early closure of the mitral valve
- Fungal endocarditis
- Annular or aortic abscess, true aneurysm of the sinus of valsalva, true or false aneurysm of the aorta
- Evidence of valvular dysfunction and persistent infection after a prolonged period (7-10 days) of appropriate antibiotics, as indicated by presence of **fever, leukocytosis, bacteraemia** – assuming that there are no non-cardiac causes for infection
- Recurrent emboli after appropriate antibiotic therapy
- Mobile vegetations >10mm diameter
- Early infection of the mitral valve – that can be repaired
- Persistent pyrexia and leukocytosis with negative blood cultures
- Relapse after an adequate course of antibiotics

### **Prosthetic**

- Early prosthetic valve endocarditis (<2 months)
- Heart failure with prosthetic valve dysfunction
- Fungal endocarditis
- Staphylococcal endocarditis unresponsive to antibiotics
- Paravalvular leak, annular or aortic root abscess
- Sinus or aortic true/false aneurysm, fistula formation
- Infection with Gram –ve organisms or organisms with a poor response to antibiotics
- Persistent bacteraemia after 7-10 days of antibiotics
- Recurrent peripheral embolus
- Vegetation on prosthesis
- New-onset conduction disturbance
- Relapse after an adequate course of antibiotics

### **Infective endocarditis**

#### **Duke criteria and terminology used in the modified diagnostic criteria**

#### **Definite infective endocarditis**

##### Pathological criteria

- Micro-organisms: demonstrated by culture or histology in a vegetation that has embolised, or in an intracardiac abscess, or
- Pathologic lesions: vegetation or intracardiac abscess present, confirmed by histology showing active endocarditis.

##### Clinical criteria (see below)

- 2 major criteria, or
- 1 major and 3 minor criteria, or
- 5 minor criteria

## Possible infective endocarditis

- Findings consistent with IE that fall short of “definite”, but not “rejected”

## Rejected

- Firm alternate diagnosis for manifestations of endocarditis, or
- Resolution of manifestations of endocarditis, with antibiotic therapy for 4 days or less, or
- No pathological evidence of IE at surgery or autopsy, after antibiotic therapy for 4 days or less

## DEFINITIONS

### Major Criteria

Positive blood culture for IE

- Isolation of micro-organism known to cause IE from two separate blood cultures eg viridans streptococci, *Strep. bovis*, *Staph. aureus*, *Staph. epidermidis*, enterococci, *Haemophilus* spp, *Actinobacillus* spp. etc
- Persistently positive blood culture – defined as recovery of a micro-organism consistent with endocarditis from:-
  - (i) at least two blood cultures drawn more than 12 hrs apart, or
  - (ii) all of three or a majority of four or more separate blood cultures, with first and last drawn at least one hr apart

Evidence of endocardial involvement

- Positive echo for IE:-
  - (i) mobile intracardiac mass on valve or supporting structures or in path of regurgitant jet, or on implanted material without any alternative anatomical explanation, or
  - (ii) abscess, or
  - (iii) new partial dehiscence of prosthetic valve, or new valve regurgitation

Clinical evidence of new valvular regurgitation

Positive serology for Q-fever and other causes of culture-negative endocarditis eg. *Bartonella* spp, *Chlamydia psittaci*.

Positive identification of a micro-organism from blood culture or excised tissue using molecular biology methods.

### Minor criteria

Predisposition: predisposing heart condition or IV drug abuse

Fever:  $>38.0^{\circ}\text{C}$

Vascular phenomena: major arterial emboli, septic pulmonary infarcts, mycotic aneurysm, intracranial haemorrhage, conjunctival haemorrhages, Janeway lesions, *newly diagnosed clubbing*, *splinter haemorrhages*, *splenomegaly*\*

Immunologic phenomena: glomerulonephritis, Osler's nodes, Roth spots, +ve rheumatoid factor, *high ESR ( $> 1.5$  times upper limit of normal)*, *high C-reactive protein level ( $>100$  mg/l)*\*

Microbiologic evidence: positive blood culture, but not meeting major criteria as defined above

\* additional modifications to the Duke criteria appear to improve diagnostic sensitivity whilst retaining specificity.

# **SURGICAL TREATMENT OF ENDOCARDITIS**

**Mr. C. Munsch – Leeds General Infirmary.**

## **Content**

- Definition and diagnosis
- Indications for Surgery
- Principles of Surgical Treatment
- Prosthetic Valve Endocarditis
- Outcomes of Treatment
- Case Study for Discussion

## **Definition and Diagnosis –Nomenclature**

- Infective Endocarditis (IE) is currently preferred term
- Native or Prosthetic Valve Endocarditis
- Community or Hospital Acquired Endocarditis
- Infecting Organism

## **Definition and Diagnosis –Duke Criteria**

- 2 Major Criteria
  - Positive Blood Culture
  - Positive Echocardiogram
- 6 Minor Criteria
  - Predisposition
  - Fever
  - Vascular Phenomena
  - Immunological Phenomena
  - Suggestive Echocardiogram
  - Suggestive Microbiology
- Diagnosis is ‘definite’, ‘possible’ or ‘rejected’

## **Echocardiography in IE**

- TOE is preferred
- TOE within 12 hrs of initial evaluation
- Repeat echo if high risk of complications or change in clinical course
- Repeat echo at 7 –10 days if diagnosis not confirmed and suspicion remains
- Intraoperative,
- Post operative
- Completion of therapy

## **Antimicrobial therapy**

# CLINICAL ANATOMY OF THE AORTIC ROOT

Mr. I. Wilson – Queen Elizabeth Hospital, Birmingham.

- **Location of the aortic root**

Although forming the outlet from the left ventricle, when viewed in the context of the heart as it lies within the chest, the aortic root is positioned to the right and posterior relative to the subpulmonary infundibulum. The subpulmonary infundibulum is a complete muscular funnel which supports in uniform fashion the leaflets of the pulmonary valve. In contrast, the leaflets of the aortic valve are attached only in part to the muscular walls of the left ventricle. This is because the aortic and mitral valvar orifices are fitted alongside each other within the circular short axis profile of the left ventricle, as compared to the tricuspid and pulmonary valves which occupy opposite ends of the banana shaped right ventricle. When the posterior margins of the aortic root are examined, then the valvar leaflets are seen to be wedged between the orifices of the two atrioventricular valves. Sections in long axis of the left ventricle then reveal the full extent of the root, which is from the proximal attachment of the valvar leaflets within the left ventricle to their distal attachments at the junction between the sinus and tubular parts of the aorta.

- **The aortic root**

Forming the outflow tract from the left ventricle, the aortic root functions as the supporting structure for the aortic valve. As such, it forms a bridge between the left ventricle and the ascending aorta. The anatomic boundary between the left ventricle and the aorta, however, is found at the point where the ventricular structures change to the fibroelastic wall of the arterial trunk. This locus is not coincident with the attachment of the leaflets of the aortic valve. The leaflets are attached within a cylinder extending to the sinutubular junction of the aorta. The semilunar attachments of the leaflets themselves form the haemodynamic junction between left ventricle and aorta. All structures distal to these attachments are subject to arterial pressures, whereas all parts proximal to the attachments are subjected to ventricular pressures.

The structures distal to the semilunar attachments are the valvar sinuses, into which the semilunar leaflets themselves open during ventricular systole. Two of these valvar sinuses give rise to the coronary arteries, usually at or below the level of the sinutubular junction. The arrangement of the coronary arteries permits these two sinuses to be called the right and left coronary aortic sinuses. When their structure is examined, it can then be seen that, for the greater part, the sinuses are made up of the wall of the aorta. At the base of each of these coronary sinuses, however, a crescent of ventricular musculature is incorporated as part of the arterial segment. This does not happen within the third, non-coronary sinus. This is because the base of this sinus is exclusively fibrous in consequence of the continuity between the leaflets of the aortic and mitral valves.

Examination of the area of the root proximal to the attachment of the valvar leaflets also reveals unexpected findings. Because of the semilunar nature of the attachments, there are three triangular extensions of the left ventricular outflow tract which reach to the level of the sinutubular junction. These extensions, however, are bounded not by ventricular musculature, but by the thinned fibrous walls of the aorta between the expanded sinuses. Each of these triangular extensions places the most distal parts of the left ventricle in potential communication with the pericardial space or, in the case of the triangle between the two coronary aortic valvar sinuses, with the tissue plane between the back of the subpulmonary infundibulum and the front of the aorta. The triangle between the left coronary and the non-coronary aortic valvar sinuses forms part of the aortic-mitral valvar curtain, with the apex of the triangle bounding the transverse pericardial sinus. The triangle between the non-coronary and the right coronary aortic valvar sinuses incorporates within it the membranous part of the septum. This fibrous part of the septum is crossed on its right side by the hinge of the tricuspid valve, which divides the septum into atrioventricular and interventricular components. The apex of the triangle, however, continuous with the atrioventricular part of the septum, separates the left ventricular outflow tract from the right side of the transverse pericardial sinus, extending above the

attachment of the supraventricular crest of the right ventricle.

When considered as a whole, therefore, the aortic root is divided by the semilunar attachment of the leaflets into supra- and subvalvar components. The supra- and subvalvar components, in essence, are the aortic sinuses, but they contain at their base structures of ventricular origin. The supporting subvalvar parts are primarily ventricular, but extend as three triangles to the level of the sinotubular junction. Stenosis at the level of the sinotubular junction is usually described as being "supra- and subvalvar". In that the peripheral attachments of the leaflets are found at this level, the junction is also an integral part of the valvar mechanism. Indeed, stretching of the sinotubular junction is one of the cardinal causes of valvar incompetence.

- **Aortic valve annulus**

The aortic annulus is the fibrous tissue to which the leaflets are attached. This is formed in the shape of a cylindrical aortic root, with the valvar leaflets supported in crown-like fashion.

- **Aortomitral Continuity**

The central fibrous skeleton of the heart includes the right fibrous trigone (the central fibrous body), the left fibrous trigone and the membranous septum.

The non-coronary leaflet straddles the central fibrous body overlying the anterior leaflet of the mitral valve. The conduction tissue traverses the membranous septum between the right coronary and non-coronary leaflets.

# AORTIC STENOSIS

**Dr. J. Townend – Queen Elizabeth Hospital, Birmingham.**

Aortic stenosis is the commonest valve lesion in developed countries. Up to 25% of the elderly (>65 years) adult population have calcific changes of the valve leaflets and 2-3% have significant obstruction to ventricular outflow. It is usually the result of an inflammatory (not degenerative) process affecting the leaflets leading to progressive thickening and calcification. The cause of this change is unknown but the risk factors are the same as those for atherosclerosis.

The normal aortic valve area is 4.0 cm<sup>2</sup>, the lesion is not said to be severe until the valve area is reduced to < 1.0 cm<sup>2</sup>. Providing left ventricular systolic function is normal, the valve gradient is almost always > 50 mmHg at this level of stenosis.

Valve gradients and areas are most easily and best assessed by echo-Doppler studies. The information provided is a maximum instantaneous gradient from which a valve area can be derived using the continuity equation. The echo gradient will always be greater than the artificial 'peak to peak' pressure drop usually given by cardiac catheterisation which is obtained by catheter 'pull back' across the valve.

The natural history is one of slow progression (mean rate of change is a reduction in area of 0.1-0.2 cm<sup>2</sup> per year) without symptoms or risk of death until symptoms occur at which time mortality is high without valve replacement.

In general, valve replacement can be safely left until the onset of symptoms even in the presence of high gradients. Careful follow up is however required if the Doppler velocity is > 4 m/s as the majority of patients will require surgery within 2 years. The degree of valve calcification is a marker of rapid progression. Exercise testing can be safely used to assess if symptoms are in doubt.

When ventricular function is poor, the valve gradient is reduced and assessment of the need and potential benefit can be difficult. The response to inotropes and vasodilators can be helpful in distinguishing those patients with a low fixed valve area (high benefit from valve replacement) from those with 'relative' aortic stenosis (probable benefit) and those with very poor left ventricular function and mild aortic stenosis (little or not benefit). This subject is well covered in reference 4.

## **Suggested Reading:**

1. Carabello B. Evaluation and management of patients with aortic stenosis. *Circulation* 2002; 105: 1746-50.
2. Otto et al. Prospective study of asymptomatic valvular aortic stenosis. *Circulation* 1997; 95: 2262-70.
3. Rosenhek R et al. Predictors of outcome in severe asymptomatic aortic stenosis. *N Engl J Med* 2000; 343: 611-17.
4. Zile MR and Gaasch WH. Heart failure in aortic stenosis – improving diagnosis and treatment. *N Engl J Med* 2003; 348: 1735-36.

# AORTIC STENOSIS

## **Mr. S. Ohri - Southampton University Hospital.**

Aortic stenosis (AS) occurs when there is obstruction to the ejection of blood from the left ventricle. It is the most common valvular pathology affecting Western World populations with an incidence of 3% in those over 75yr. In adults, AS is usually caused by degenerative (calcific) disease. Aortic stenosis is a slowly progressive disease, with patients remaining asymptomatic for many years. The development of symptoms, including angina, syncope and congestive heart failure, marks a prognostic turning-point in the natural history of the disease and is characterized by increased mortality without surgical intervention. Until recently, surgery even for *asymptomatic* severe AS (Doppler flow  $\geq 4.5\text{m/s}$ ) was controversial; new evidence now supports a surgical approach.

The aetiology of calcific degeneration of the valve is undergoing rigorous investigation. Pathologic similarities exist between the leaflet plaques of AS and atherosclerotic plaques, except that atheroma is characterised by monoclonal smooth cell proliferation and lipid-laden macrophages. Retrospective observational studies have found a reduction in AS and bioprosthetic valvular degeneration with statin therapy, but this is not supported by recent randomized research.

Echocardiography has emerged as the principle method for establishing the diagnosis and allowing assessment of aortic valve anatomy, the severity of valvular obstruction and the left ventricular response to pressure overload. The co-existence of coronary disease and AS has spurred the debate surrounding the timing of valve replacement in those patients with mild (valve area  $>1.5\text{cm}^2$ ) or moderate (valve area  $1.0\text{-}1.5\text{cm}^2$ ) AS. The rate of AS progression may be key in the decision making process, but the rate of change is often unavailable at the time of CABG.

Further controversy surrounds surgical intervention for those patients with significant AS and impaired LV function. The historic guidance that all patients with impaired LV function benefit has now being further refined with the advent of dobutamine stress echocardiography and gadolinium enhance MRI. Patients with flow reserve with stress echo have superior prognosis, but a proportion of those without significant flow reserve will still improve following valve replacement. Identification of the latter group will undoubtedly enhance surgical selection and avoid unnecessary surgical mortality.

# **PATIENT PROSTHESIS MISMATCH IN AORTIC VALVE**

## **REPLACEMENT:**

### **POSSIBLE BUT PERTINENT?**

**Professor D. Taggart – John Radcliffe Hospital, Oxford.**

Aortic valve replacement (AVR) is now the second most commonly performed cardiac operation and with a rising elderly population the number of such procedures is increasing. More than a quarter of a century ago Rahimtoola coined the term Patient Prosthesis Mismatch (PPM) to describe the situation in which the effective orifice area of a prosthetic valve is smaller than that of the native valve [1]. Initially PPM did not attract much attention because at that time operative mortality and more overt morbidity were much more immediate and relevant issues. Furthermore, over 90% of AVR performed today still use a prosthesis with a sewing ring and by definition must have at least some degree of PPM. Finally as many patients can tolerate at least moderate aortic stenosis with excellent functional status and well preserved ventricular function over long periods without the need for surgery, the clinical relevance of PPM is uncertain.

In the last decade, however, Pibarot and colleagues more precisely sub-classified PPM according to the effective orifice index area of a prosthetic valve as mild ( $>0.85\text{cm}^2/\text{m}^2$ ), moderate ( $0.65 - 0.85\text{cm}^2/\text{m}^2$ ) or severe ( $<0.65\text{cm}^2/\text{m}^2$ ) [2,3]. Since then, the cardiac surgical literature has become increasingly concerned with the possible adverse effects of PPM on short and long term survival as well as functional status. However, surgical procedures designed to enlarge the aortic root to avoid PPM increase the complexity of the operation and its operative mortality even in the best centres. So is there compelling evidence that the potential detrimental effects of PPM merit the performance of more complex and higher risk operations ?.

#### **1. Two important considerations regarding PPM and outcome**

The question of whether PPM impacts adversely on clinical outcome may initially appear straightforward but in reality is bedeviled by two facts. First, and most importantly, patients at the highest risk of PPM are those who are already also at the highest risk from surgery. PPM is most likely to occur in patients with small aortic roots who accordingly receive smaller prosthetic valves. This scenario is most probable in the elderly (especially females) who are also more likely to have severe coronary artery disease and poorer cardiac function and are therefore already at a higher risk from surgery. Even multivariate analysis can only partially, at best, discriminate between these confounding factors.

A second complicating factor is the now well recognized, albeit counter-intuitive, fact that there can be marked discrepancies between the manufacturer labeled and actual diameter of the valve prosthesis [4-6]. Failure to appreciate this has almost certainly contributed to a frequent inability in the literature to relate labeled size of valves to haemodynamic performance.

#### **2. PPM and short term survival from AVR**

The strongest evidence implying that that PPM has an important adverse influence on operative mortality following AVR is by Pibarot's group. In 1266 consecutive AVR patients the overall 30 day mortality was 4.6%. However in 38% of patients with moderate or severe PPM the relative risk of mortality was increased two fold in patients with moderate PPM and eleven fold in those with severe PPM. Although the authors reported that comorbid factors such as older age, female gender, coronary artery disease, hypertension, diabetes, and emergent/salvage operation were more prevalent in patients with moderate and severe PPM and might have contributed to the higher mortality in these patients they still went on to conclude that PPM is a strong and independent predictor of short-term mortality among patients undergoing AVR.

Few other studies have identified such an adverse effect of PPM on operative outcome. Indeed Blackstone and colleagues study of the effect of PPM on operative outcome in over 13000 patients undergoing AVR found.....

#### **3. PPM and long term survival from AVR**

The most definitive study on the potential effects of PPM on long term survival was by

Blackstone and colleagues in a study of over 13 000 patients undergoing aortic valve replacement and followed for up to 15 years. After adjustment for other preoperative risk factors the authors could identify no effect of PPM on survival. This study reinforces the findings of several other studies. Similarly, Hanayama and colleagues, in a study of almost 700 patients undergoing aortic valve replacement and followed for 10 years, could find no effect of even severe PPM on survival. Indeed 3 other studies (see Table 1) could find no effect on long term outcome.

#### **4. PPM and cardiac failure after AVR.**

Ruel and colleagues reported PPM (defined as an effective orifice area of less than  $0.80\text{cm}^2/\text{m}^2$ ) as an independent predictor of post operative congestive heart failure in over 1500 patients undergoing AVR. with with, but interestingly had no effect on survival. Interestingly enough, when a slightly different cut-off value was used, less than  $0.85\text{cm}^2/\text{m}^2$ , the association between mismatch and heart failure disappeared.

#### **5. PPM and functional recovery after AVR**

This question was recently addressed in a study from the Cleveland Clinic in 1108 patients undergoing aortic valve replacement and whose functional post-operative recovery was assessed by the Duke Activity Status Index (DASI) at 8 months after surgery. Overall there was a significant improvement in post operative functional recovery in all patients, but no measure of valve orifice area could be correlated with functional recovery. On the other hand, female sex, increasing age and pre-operative renal impairment are associated with a poor functional recovery.

#### **6. Surgical options and risks for avoiding PPM**

The potential risk of PPM has led several authors to recommend maneuvers to enlarge the aortic annulus or root. While these procedures may be technically successful in permitting implantation of a larger sized prosthesis they also increase the complexity of the procedure and, more importantly, the operative risk, particularly as those who are most likely to have PPM are those who have the smallest roots, in other words elderly females. Even in the best hands enlargement of the aortic root often can transform a straightforward operation into a more complex procedure as witnessed by a significant increase in mortality.

#### **7. Summary and conclusions.**

Most patients undergoing prosthetic AVR will have some degree of PPM because the presence of a sewing ring makes most aortic valve prostheses by definition inherently stenotic. While intuitively PPM might be felt to adversely effect operative outcome, and functional activity or survival the best evidence shows that in the vast majority it is of little clinical relevance. This however is consistent with the observation that asymptomatic patients can have severe aortic stenosis (defined as an area less than  $0.6\text{cm}^2/\text{m}^2$ ) and remain asymptomatic with good long term outcome. as long as they are.

Even in the small cohort of patients with potentially severe PPM there is still little substantial evidence that this has an important adverse effect on short or long term functional recovery or survival. However, the increased risks of enlarging the aortic roots in such patients, who are usually elderly and with small aortic roots and who are already at the highest risk from surgery, should therefore be carefully considered – especially as most will do well with less than a perfect result because activities are already limited.

[Blais C, Dumesnil JG, Baillot R, Simard S, Doyle D, Pibarot P.](#) Impact of valve prosthesis-patient mismatch on short-term mortality after aortic valve replacement. *Circulation.* 2003;108:983-8.

but then added , and its impact is related both to its degree of severity and the status of left ventricular function. In contrast to other risk factors, moderate-severe PPM can be largely avoided with the use of a prospective strategy at the time of operation.

*J Thorac Cardiovasc Surg.* 2003 Sep;126(3):783-96.

- [J Thorac Cardiovasc Surg.](#) 2004 Jun;127(6):1852; author reply 1852-4.

## **Prosthesis size and long-term survival after aortic valve replacement.**

[Blackstone EH](#), [Cosgrove DM](#), [Jamieson WR](#), [Birkmeyer NJ](#), [Lemmer JH Jr](#), [Miller DC](#), [Butchart EG](#), [Rizzoli G](#), [Yacoub M](#), [Chai A](#).

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**OBJECTIVE:** This study was undertaken to quantify the relationship between prosthesis size adjusted for patient size (prosthesis-patient size) and long-term survival after aortic valve replacement. **METHODS:** Data from nine representative sources on 13,258 aortic valve replacements provided 69,780 patient-years of follow-up (mean 5.3 +/- 4.7 years), with reliable survival estimates to 15 years. Prostheses included 5757 stented porcine xenografts, 3198 stented bovine pericardial xenografts, 3583 mechanical valves, and 720 allografts. Manufacturers' labeled prosthesis size was 19 mm or smaller in 1109 patients. Expressions of prosthesis-patient size assessed were indexed internal prosthesis orifice area (in centimeters squared per square meter of body surface area) and standardized internal prosthesis orifice size (Z, the number of SDs from mean normal native aortic valve size). Multivariable hazard domain analysis with balancing score and risk factor adjustment quantified the association of prosthesis-patient size with survival. **RESULTS:** Prosthesis-patient size down to at least 1.1 cm<sup>2</sup>/m<sup>2</sup> or -3 Z did not adversely affect intermediate- or long-term survival (P >.2). However, 30-day mortality increased 1% to 2% when indexed orifice area fell below 1.2 cm<sup>2</sup>/m<sup>2</sup> (P =.002) or standardized orifice size fell below -2.5 Z (P =.0003). The increased early risk affected fewer than 1% of patients receiving bioprostheses but about 25% of those receiving mechanical devices. **CONCLUSIONS:** Aortic prosthesis-patient size down to 1.1 cm<sup>2</sup>/m<sup>2</sup> or -3 Z did not reduce intermediate- or long-term survival after aortic valve replacement. However, patient-prosthesis size under 1.2 cm<sup>2</sup>/m<sup>2</sup> or -2.5 Z was associated with a 1% to 2% increase in 30-day mortality. Prosthesis-patient sizes this small or smaller were rarely implanted in patients receiving bioprostheses.

Ann Thorac Surg. 2002 Jun;73(6):1822-9; discussion 1829.

**Patient prosthesis mismatch is rare after aortic valve replacement: valve size may be irrelevant.**

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**BACKGROUND:** Although small valve size and patient-prosthesis mismatch are both considered to decrease long-term survival, little direct evidence exists to support this hypothesis. **METHODS:** To assess the prevalence of patient-prosthesis mismatch and the influence of small valve size on survival, we prospectively studied 1,129 consecutive patients undergoing aortic valve replacement between 1990 and 2000. Mean and peak gradients and indexed effective orifice area were measured by transthoracic echocardiography postoperatively (3 months to 10 years). Abnormal postoperative gradients were defined as those patients with mean or peak gradient above the 90th percentile (mean gradient  $\geq 21$  or peak gradient  $\geq 38$  mm Hg). Patient-prosthesis mismatch was defined as those patients with indexed effective orifice area below the 10th percentile ( $< 0.60$  cm<sup>2</sup>/m<sup>2</sup>). **RESULTS:** A multivariable analysis identified internal diameter of the implanted valve as the only independent predictor of abnormal gradients postoperatively. However, there was no significant difference in actuarial survival between normal and abnormal gradient groups (7 years: 91.2%  $\pm$  1.5% versus 95.0%  $\pm$  2.2%;  $p = 0.48$ ). Freedom from New York Heart Association class III or IV (7 years: 74.5%  $\pm$  3.1% versus 74.6%  $\pm$  6.2%;  $p = 0.66$ ) and left ventricular mass index were not different between normal and abnormal gradient groups. Patients with and without patient-prosthesis mismatch were similar with respect to postoperative left ventricular mass index, 7-year survival (95.1%  $\pm$  1.3% versus 94.7%  $\pm$  3.0%;  $p = 0.54$ ), and 7-year freedom from New York Heart Association class III or IV (79.3%  $\pm$  6.6% versus 74.5%  $\pm$  2.5%;  $p = 0.40$ ). In patients with patient-prosthesis mismatch and abnormal gradients, the majority had prosthesis dysfunction owing to degeneration. **CONCLUSIONS:** Severe patient-prosthesis mismatch is rare after aortic valve replacement. Patient-prosthesis mismatch, abnormal gradient, and the size of valve implanted do not influence left ventricular mass index or intermediate-term survival.

Circulation. 2000 Nov 7;102(19 Suppl 3):III5-9.

## **Prosthesis-patient mismatch affects survival after aortic valve replacement.**

[Rao V, Jamieson WR, Ivanov J, Armstrong S, David TE.](#)

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**BACKGROUND:** Surgeons traditionally avoid the use of "small" aortic prostheses because of the potential for residual left ventricular outflow tract obstruction and persistent transvalvular gradients. This study examines the ratio between prosthetic valve size and the body surface area (BSA) of patients undergoing aortic valve replacement (AVR). We sought to determine the effect of potential "prosthesis-patient" mismatch on long-term survival. **METHODS AND RESULTS:** Follow-up was conducted on 2981 patients who underwent AVR with stented bioprostheses between 1976 and 1996. To account for differences between manufacturers' labeled valve sizes, we calculated the ratio between the prosthetic valve effective orifice area (EOA) and the patient's BSA (recorded for 2154 patients). The lowest decile in this cohort had a calculated EOA/BSA of  $<0.75 \text{ cm}^2/\text{m}^2$  (Small group,  $n=227$ ) compared with the control group ( $n=1927$ ), in whom the EOA/BSA ratio was  $>0.75 \text{ cm}^2/\text{m}^2$ . Operative mortality was higher in the Small group (8% versus 5%,  $P=0.03$ ). Actuarial survival at 12 years was  $50\pm 5\%$  in the Small group compared with  $49\pm 2\%$  in the control group ( $P=0.27$ ). However, freedom from valve-related mortality was significantly lower in the Small group ( $75\pm 5\%$  versus  $84\pm 2\%$ ,  $P=0.004$ ). Cox regression analysis determined age and NYHA functional class to be the multivariate predictors of overall mortality, whereas advanced age and EOA/BSA  $<0.75 \text{ cm}^2/\text{m}^2$  were found to be the predictors of valve-related mortality. **CONCLUSIONS:** Prosthesis-patient mismatch results in significantly higher early and late mortality after bioprosthetic AVR. We recommend careful selection of stented bioprostheses to ensure an adequate ratio of EOA to BSA. An EOA/BSA ratio of  $>0.75 \text{ cm}^2/\text{m}^2$  may avoid residual left ventricular outflow tract obstruction and persistent transvalvular gradients. Careful prosthesis-patient matching will improve both early and late survival after AVR.

Can J Cardiol. 1996 Apr;12(4):379-87.

## **The effect of prosthesis-patient mismatch on aortic bioprosthetic valve hemodynamic performance and patient clinical status.**

**Pibarot P, Honos GN, Durand LG, Dumesnil JG.**

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**BACKGROUND:** High pressure gradients occurring through normally functioning prosthetic valves appear to be related to a mismatch between the effective orifice area of the prosthesis and the patient's body surface area. **OBJECTIVE:** To determine whether prosthesis-patient mismatch affects clinical and hemodynamic status, a group of patients with a bioprosthetic heart valve in the aortic position was prospectively evaluated at 6.2±4.4 years after implantation by transthoracic Doppler echocardiography. **METHODS:** Manufacturer-derived in vitro valve areas were available in 61 patients allowing classification into two subgroups, with or without mismatch, based on a valve area at implantation indexed for body surface area 0.85 cm<sup>2</sup>/m<sup>2</sup> or less, or greater than 0.85 cm<sup>2</sup>/m<sup>2</sup>. Clinical and hemodynamic parameters evaluated at follow-up included New York Heart Association (NYHA) class distribution, mean transprosthetic gradient, prosthetic valve area and cardiac index. **RESULTS:** Prosthesis-patient mismatch was present in 32 of 61 patients (52%). Although NYHA class of the patients was similar in both groups, hemo-dynamic performance of the aortic bioprostheses was worse in patients with mismatch than in patients with no mismatch, as indicated by a higher mean gradient (22±9 versus 15±8 mm Hg, P=0.002) and a lower cardiac index (3.0±0.7 versus 3.4±0.7 L/min/m<sup>2</sup>, P=0.04). The prevalence and severity of intrinsic prosthetic dysfunction were similar in both groups. Despite similar NYHA functional class distribution in both groups, the occurrence of syncope, acute pulmonary edema and angina pectoris was significantly higher in patients with mismatch (50% versus 21%, P=0.017). **CONCLUSIONS:** Prosthesis-patient mismatch is associated with worse hemodynamic performance and higher prevalence of adverse clinical events. However, mismatch did not promote accelerated hemodynamic or structural deterioration of the bioprosthesis.

Can J Cardiol. 1996 Apr;12(4):379-87.



# **The effect of prosthesis-patient mismatch on aortic bioprosthetic valve hemodynamic performance and patient clinical status.**

**Pibarot P, Honos GN, Durand LG, Dumesnil JG.**

Institut de recherches cliniques de Montreal, Quebec. pibarop@ircm.umontreal.ca

**BACKGROUND:** High pressure gradients occurring through normally functioning prosthetic valves appear to be related to a mismatch between the effective orifice area of the prosthesis and the patient's body surface area. **OBJECTIVE:** To determine whether prosthesis-patient mismatch affects clinical and hemodynamic status, a group of patients with a bioprosthetic heart valve in the aortic position was prospectively evaluated at 6.2±4.4 years after implantation by transthoracic Doppler echocardiography. **METHODS:** Manufacturer-derived in vitro valve areas were available in 61 patients allowing classification into two subgroups, with or without mismatch, based on a valve area at implantation indexed for body surface area 0.85 cm<sup>2</sup>/m<sup>2</sup> or less, or greater than 0.85 cm<sup>2</sup>/m<sup>2</sup>. Clinical and hemodynamic parameters evaluated at follow-up included New York Heart Association (NYHA) class distribution, mean transprosthetic gradient, prosthetic valve area and cardiac index. **RESULTS:** Prosthesis-patient mismatch was present in 32 of 61 patients (52%). Although NYHA class of the patients was similar in both groups, hemo-dynamic performance of the aortic bioprostheses was worse in patients with mismatch than in patients with no mismatch, as indicated by a higher mean gradient (22±9 versus 15±8 mm Hg, P=0.002) and a lower cardiac index (3.0±0.7 versus 3.4±0.7 L/min/m<sup>2</sup>, P=0.04). The prevalence and severity of intrinsic prosthetic dysfunction were similar in both groups. Despite similar NYHA functional class distribution in both groups, the occurrence of syncope, acute pulmonary edema and angina pectoris was significantly higher in patients with mismatch (50% versus 21%, P=0.017). **CONCLUSIONS:** Prosthesis-patient mismatch is associated with worse hemodynamic performance and higher prevalence of adverse clinical events. However, mismatch did not promote accelerated hemodynamic or structural deterioration of the bioprosthesis.

**1:** J Thorac Cardiovasc Surg. 2004 Jan;127(1):149-59.

## **Late incidence and predictors of persistent or recurrent heart failure in patients with aortic prosthetic valves.**

[Ruel M](#), [Rubens FD](#), [Masters RG](#), [Pipe AL](#), [Bedard P](#), [Hendry PJ](#), [Lam BK](#), [Burwash IG](#), [Goldstein WG](#), [Brais MP](#), [Keon WJ](#), [Mesana TG](#).

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**BACKGROUND:** We examined factors associated with persistent or recurrent congestive heart failure after aortic valve replacement. **METHODS:** Patients who underwent aortic valve replacement with contemporary prostheses (n = 1563) were followed up with annual clinical assessment and echocardiography. The effect of demographic, comorbid, and valve-related variables on the composite outcome of New York Heart Association class III or IV symptoms or congestive heart failure death after surgery was evaluated with stratified log-rank tests, Cox proportional hazard models, and logistic regression. Factors associated with all-cause death were also examined. Prediction models were bootstrapped 1000 times. **RESULTS:** Total follow-up was 6768 patient-years (mean, 4.3 +/- 3.3 years; range, 60 days to 17.1 years). Freedom from congestive heart failure or congestive heart failure death was 98.6% +/- 0.3%, 88.6% +/- 1.0%, 73.9% +/- 2.3%, and 45.2% +/- 8.5% at 1, 5, 10, and 15 years, respectively. Age, preoperative New York Heart Association class, left ventricular grade, atrial fibrillation, coronary artery disease, smoking, and redo status predicted congestive heart failure after surgery (all P <.05). Larger prosthesis size and effective orifice area, both absolute and indexed for body surface area, were independently associated with freedom from congestive heart failure. Increased transprosthesis gradients were predicted by prosthesis-patient mismatch and were associated with congestive heart failure after surgery. Mismatch defined as an effective orifice area/body surface area of 0.80 cm(2)/m(2) or less was a significant predictor of congestive heart failure events after surgery, but mismatch defined as an effective orifice area/body surface area of 0.85 cm(2)/m(2) or less was not. Small prosthesis size and mismatch were not significantly associated with all-cause mortality. **CONCLUSIONS:** These analyses identify independent predictors of congestive heart failure symptoms and congestive heart failure death late after aortic valve replacement and indicate that prosthesis size has a significant effect on this cardiac end point, but not on overall survival after aortic valve replacement.

## **Influence of patient-prosthesis mismatch on long-term results after aortic valve replacement with a stented bioprosthesis.**

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**BACKGROUND AND AIMS OF THE STUDY:** The study aim was to compare long-term results of bioprostheses implanted in the aortic position, with and without patient-prosthesis mismatch (defined as effective orifice area (EOA)/body surface area (BSA)  $<$  or  $=0.85$  cm<sup>2</sup>/m<sup>2</sup>). **METHODS:** Between 1986 and 1990, 90 consecutive patients (mean age 72.6 years; mean BSA 1.77 $\pm$ 0.2 m<sup>2</sup>) each received an aortic Medtronic Intact valve (19 mm, n = 35; 21 mm, n = 29;  $>$ 23 mm, n = 26). Of these patients, 64 had a patient-prosthesis mismatch, and 26 had no mismatch. Median follow up was 7.3 years. **RESULTS:** At 10 years postoperatively, there was no significant inter-group difference in actuarial freedom from thromboembolism (90.7% in mismatch group, 79.6% in no-mismatch group; p = 0.16), hemorrhage (86% versus 83.3%; p = 0.59), endocarditis (98.2% versus 86.7%; p = 0.1), structural valve deterioration (97% versus 100%; p = 0.57) and reoperation (96.4% versus 94.8%; p = 0.2). At the same time, overall actuarial survival was 42.1 $\pm$ 6.5% in the mismatch group and 22.6 $\pm$ 8.6% in the no-mismatch group (p = 0.08). By multivariate analysis, the main risk factor for late death was a preoperative left ventricular ejection fraction (LVEF)  $<$ 50% (p = 0.001). Freedom from cardiac death was 70 $\pm$ 6% and 35.7 $\pm$ 11% in the mismatch and no-mismatch groups respectively (p = 0.005), but this was not significantly different when LVEFs were paired (LVEF  $>$ 50% p = 0.33, LVEF  $<$ 50% p = 0.28). The NYHA functional status of survivors showed 94.4% of the mismatch group and 100% of the no-mismatch group to be in NYHA classes I and II (p = 1). **CONCLUSION:** Within this patient population it was not possible to demonstrate any negative effects of patient-prosthesis mismatch at 10 years after Intact aortic valve replacement; the LVEF was the only predictor for late death.

J Thorac Cardiovasc Surg. 2000 May;119(5):963-74.

## **Aortic valve replacement: is valve size important?**

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**OBJECTIVE:** We sought to determine whether aortic prosthesis size adversely influences survival after aortic valve replacement. **METHODS:** A total of 892 adults receiving a mechanical (n = 346), pericardial (n = 463), or allograft (n = 83) valve for aortic stenosis were observed for up to 20 years (mean, 5.0 +/- 3.9 years) after primary isolated aortic valve replacement. We used multivariable propensity scores to adjust for valve selection factors, multivariable hazard function analyses to identify risk factors for all-cause mortality, and bootstrap resampling to quantify the reliability of the results. **RESULTS:** Twenty-five percent of patients had indexed internal orifice areas of less than 1.5 cm<sup>2</sup>/m<sup>2</sup> and more than 2 SDs (Z-value) below predicted normal aortic valve size. Mechanical valve orifices were smaller (1.3 +/- 0.29 cm<sup>2</sup>/m<sup>2</sup>, Z = -2.2 +/- 1.16) than pericardial (1.9 +/- 0.36 cm<sup>2</sup>/m<sup>2</sup>, Z = -0.40 +/- 1.01) or allograft valves (2.1 +/- 0.50, Z = 0.24 +/- 1.17). The overall survival was 98%, 96%, 86%, 69%, and 49% at 30 days and 1, 5, 10, and 15 years postoperatively. Univariably, survival was weakly and inversely related to manufacturer valve size (P = .16) and internal orifice diameter (P = .2) but completely unrelated to indexed valve area (P = .6) or Z-value (P = .8). These, and univariable differences among valve types (P = .004), were accounted for by different prevalences in patient risk factors and not by valve size or type per se. Bootstrap resampling indicated that these findings had a less than 15% chance of being incorrect. **CONCLUSIONS:** Survival after aortic valve replacement is strongly related to patient risk factors but appears not to be adversely affected by moderate patient-prosthesis mismatch (down to about 4 SDs below normal). Aortic root enlargement to accommodate a large prosthesis may be required in few situations.

# AORTIC REGURGITATION

## - THE EVIDENCE BASE

**Mr. S. Kendall – James Cook University Hospital, Middlesbrough.**

Chronic Aortic Regurgitation may be asymptomatic with preserved LV function; of these patients, 6% will develop LV dysfunction of which 25% will not develop symptoms. Therefore all patients should be reviewed every 6-12 months with echocardiography and referred for surgery if there is evidence of LV dilation; LVEDD >70mm or the LVESD >50mm. Symptomatic patients with moderate or severe AR require AVR, but if symptomatic with mild AR (+/- LV dysfunction) then other causes must be excluded.

1. Symptomatic patients with severe / moderate AR are referred for surgery to treat their symptoms.
2. Asymptomatic patients with severe AR are referred for surgery if there is evidence of LV dysfunction, as progressive dysfunction is inevitable and the risk of surgery will increase.  
If LV function is normal then the patients must be regularly reviewed with echocardiography. Surgery is not immediately indicated because the deterioration of the LV function is not predictable.
3. Prosthetic valve dysfunction. This category includes: severe paravalvular leak; small paravalvular leak causing significant haemolysis; mechanical valve thrombus / leaflet dysfunction; deterioration of a biological valve (chronic and acute). These conditions all require surgery.
4. AR as an incidental finding prior to other cardiac surgery should be considered for surgical correction.
5. AR is associated with ascending aortic aneurysms.

Acute Aortic Regurgitation requires 'in-house' / emergency surgery.

1. Aortic Dissection. Displacement of the commissures by intramural haematoma causes AR and requires correction.
2. Aortic valve endocarditis. If the organism can be treated and the patient remains stable then surgery is deferred until the organism is eradicated. Surgery is precipitated by; unstable cardiovascular status; progression of abscess; likelihood of further emboli.
3. Traumatic. Occasionally occurs in blunt trauma, and if missed presents as chronic AR.
4. Iatrogenic. Occasionally following ; mitral valve surgery due to a deep suture; damage by cardioplegia cannula.
5. Rupture of a leaflet in a prosthetic biological valve.

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# AORTIC VALVE REPAIR

Professor H.-J. Schäfers – Homburg, Germany.

Repair of the regurgitant aortic valve has been attempted as early as 40 years ago, but only in the past years improved understanding of the mechanisms of aortic regurgitation has made reconstructive surgery possible.

Regurgitation of the aortic valve may be due to root dilatation, cusp prolapse, or cusp retraction. Different pathologies may coexist, and upon careful inspection, a combination is found in the majority of patients. Similar to mitral repair, surgical correction should probably address all components that are present.

Root dilatation can be corrected by valve reimplantation within a vascular graft, root remodeling, or subcommissural placcation. Cusp prolapse can be corrected by triangular correction or simple plication. Deficiency or retraction of cusp tissue requires cusp augmentation, i.e. using autologous pericardium.

We have explored the possibilities and limits of aortic valve repair over 10 years. With systematic repair approaches repair is possible in more than 70% of patients with aortic regurgitation, 5 year freedom from reoperation is better than 90%. Operative mortality is not increased over valve replacement, the incidence of valve-related complications, such as endocarditis or thromboembolic problems has been low. Most importantly, endocarditis has been amenable to conservative therapy.

Aortic valve repair is a new and promising treatment option for patients with aortic regurgitation. Mid-term stability is similar to the more established result of mitral repair procedures.

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# **NEUROPROTECTION IN CARDIAC SURGERY**

**Professor W. A. Baumgartner – The John Hopkins Hospital, Baltimore, U.S.A.**

Several hundred thousand patients in the United States undergo cardiac surgery. The most common procedures include those for coronary artery disease, valvular heart disease, aortic disease, surgery for heart failure, congenital heart disease, transplantation, and a variety of other combined procedures. Neurologic injury is a significant risk factor for patients undergoing cardiac surgery. Although stroke, with an incidence of 1% to 6%, is the most serious complication, cognitive impairment (25% to 65%) and impaired level of consciousness (approximately 10%) can be significantly troublesome for patients and lead to potential further complications [1]. This latter complication can consist of encephalopathy, delirium, confusion, and depression. Atherosclerotic emboli from the aorta and great vessels and hypoperfusion to watershed regions of the brain are the predominant causes of stroke (or cerebrovascular accident). The cause of cognitive impairment and impaired level of consciousness is multifactorial and has been attributed to hyperperfusion, microemboli, metabolic derangements, general anesthesia, and initiation of a proinflammatory state.

## **Development of Neuroprotective Strategies**

At our institution we believe there is sufficient direct and indirect evidence to support neuroprotective strategies outlined in Table 1. The fact that the overall stroke rate for most cardiac surgical procedures has not increased during the past several years, despite a steady increase in the number of elderly patients, is in part attributed to the successful application of these strategies.

The majority of these strategies are designed to reduce potential microemboli as well as relative hypoperfusion and ischemia, which could play a role in reducing overall neurologic injury, particularly that of encephalopathy. In our own experience looking at 2,244 consecutive patients (all procedures) who did not have a stroke or encephalopathy, the hospital mortality was 1.4%. Patients who sustained a cerebrovascular accident had a mortality of 22%, whereas those with encephalopathy had a hospital mortality of 7.5%. These outcomes have been a stimulus for us to not only carefully follow our patients who have had a neurological injury but also develop a basic laboratory strategy to understand the mechanism of neurologic injury.

## **Summary of Laboratory Experience**

Since 1992, we have had continuous National Heart, Lung, and Blood Institute funding (NS31238-10) to investigate the mechanism of neurologic injury in a clinically relevant canine model of cardiopulmonary bypass and hypothermic circulatory arrest (HCA). Dogs undergo 2 hours of HCA at 18°C followed by resuscitation and recovery for 3 days. We have had wonderful collaboration with our neuroscientists, cardiologists and radiologist.

Figure 1 summarizes our current thoughts regarding the role of excitotoxicity in the mechanism of

injury. Excitotoxicity is the excessive activation of glutamate receptors that mediates neuronal injury or death [2]. We have demonstrated that the damaging role of excessive glutamate in this model. We have shown there is an elevation of glutamate above baseline levels and that when an *N*-methyl-D-aspartate (NMDA; glutamate) receptor antagonist (MK801) or  $\alpha$ -amino-3-hydroxy-5-methyl-4-isoxazolepropionic acid (AMPA) antagonist (NBQX) is administered, the excitotoxic response can be significantly blocked [3]. We have also demonstrated that neuronal nitric oxide plays a significant neurotoxic role in the injury induced by HCA. Nitric oxide synthase converts oxygen plus arginine to citrulline plus nitric oxide. Using a microdialysis technique, elevations of citrulline in the cerebrospinal fluid correlated with increased levels within cortical homogenates during HCA and reperfusion [4, 5]. This proof of concept was further validated when a number of inhibitors to neuronal nitric oxide synthase were used in this investigative model. Two specific neuronal nitric oxide synthase inhibitors (7-nitroindazole and Astra 17477AR) resulted in superior neurologic function compared with untreated HCA dogs [6].

Figure 2 further elaborates our investigations into the mechanism of injury on the subcellular level. Nitric oxide and peroxynitrite injure the mitochondria, leading to a proliferation of free radicals, which further break down cellular membranes resulting in necrosis. Apoptosis is also produced when cytochrome *c* is activated on injury to the mitochondrion, which then triggers the caspase system leading to DNA fragmentation and resultant programmed cell death.

On the basis of previous cardiac investigations with ischemic preconditioning, we performed a series of experiments with the aim that preischemic conditioning could be activated using pharmacologic agents. Certain pharmacologic agents can open adenosine triphosphate (ATP)-sensitive potassium channels on the inner membrane of the mitochondria, thereby chemically producing preconditioning leading to neuronal cell protection. Diazoxide has been shown to be a mitochondrial potassium-channel opener. By administering this drug before and during cardiopulmonary bypass, we demonstrated significant improvement in both functional scoring and histopathologic analysis in these animals compared with control animals [7].

Table 1. Neuroprotective Strategies Used in Cardiac Surgery

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Prevent hyperthermia (>37 <sup>0</sup> C) during rewarming
Use arterial line filters
Avoid rapid rewarming after hypothermic CPB
Avoid hypoglycemia as much as possible
Minimize aortic manipulation
Use of epiaortic scanning to detect unrecognized aortic atheroma
Use alpha-stat pH management for CPB in adults
Strive for Hct of 30% rather than 20%
Avoid introduction of emboli and fat globules by cardiotomy suction
Minimize neuronal excitotoxicity (future applications)

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CPB = cardiopulmonary bypass; Hct = hematocrit.

## Summary of Laboratory Experience and Future Investigative Plans

Using an animal model with significant neuronal cell injury (HCA), the following conclusions can be drawn:

Glutamate excitotoxicity occurs and contributes to the injury [3].

Fig 1. Diagram illustrating the excitotoxicity mechanism of neuronal cell injury and points of intervention. NBQXIS an  $\alpha$ -amino-3-hydroxy-5-methyl-4-isoxazolepropionic acid (AMPA) receptor antagonist; MK801 is an N-methyl-D-aspartate (NMDA) receptor antagonist; 7-nitroindazole, monosialoganglioside GM<sub>1</sub>, and Astra 17477AR are pharmacologic drugs that exhibit inhibition of nitric oxide (NO) synthase.

*(Reprinted from Baumgartner WA. Neurologic injury after cardiopulmonary bypass surgery, J Neurosurg Anesthesiol 2004; 16: 102-4 by permission of Lippincott Williams & Wilkins)*

Fig 2. Diagram illustrating the role of the mitochondria in neuronal cell injury and the mechanism of pharmacologically induced preconditioning. Diazoxide influences the opening of the adenosine triphosphate-sensitive potassium (K<sub>ATP</sub>) channels in the inner membrane of mitochondria. (NMDA = N-methyl-D-aspartate; NO nitric oxide;

NOS = nitric oxide synthase). (Reprinted from Baumgartner WA. Neurologic injury after cardiopulmonary bypass surgery, *J Neurosurg Anesthesiol* 2004; 16: 102-4 by permission of Lippincott Williams & Wilkins)

Inhibition of glutamate excitotoxicity significantly reduces this injury (functionally, receptor autoradiographically, and histopathologically) [3]

Nitric oxide is induced by hypothermic circulatory arrest [4-6]

Mitochondrial ATP-dependant potassium channels are involved in neuroprotection [7].

Our focus in the laboratory will continue to further define the mechanism of neuronal cell injury as well as investigating pharmacologic agents that block the pathway of injury at different levels. The more that is understood about the molecular and cellular pathways, the more likely we will be able to develop a specific pharmacologic approach to reducing this injury as well as a gene-screening approach to identify the high-risk patient.

### **Clinical Research Into Neurologic Injury**

Along with our colleagues in neurology, we have been evaluating neurocognitive outcomes in patients undergoing coronary artery bypass grafting (CABG). In a four-arm nonrandomized study, patient groups included those with conventional CABG with cardiopulmonary bypass, nonsurgical control patients with a diagnosis of coronary artery disease, those patients undergoing off-pump CABG, and a normal control group without known risk factors for cerebrovascular disease. We have not completed follow-up of our patients who underwent off-pump CABG, but evidence suggests that this modification of CABG might be beneficial to reducing neurologic injury in high-risk patients [8].

The majority of reports clearly demonstrate that there is a subset of patients who suffer postoperative cognitive decline [9]. Our own studies as well as those from Duke University document decline at 5 years from preoperative levels [10, 11]. The majority of studies, including our own, have focused on defining incidence and cause, but not duration.

The question is whether these early cognitive changes continue long after the operation and are the direct result of cardiopulmonary bypass. In previous studies there were no comparable groups that were controlled for cardiopulmonary bypass, anesthesia, normal aging, and vascular and other comorbid disease as well as dementia.

In previously published study [12], results were presented comparing 140 patients who underwent CABG with standard cardiopulmonary bypass with a demographically similar nonsurgical control group with documented coronary artery disease. There was no difference in mean test scores between groups at baseline, 3 months, or 1 year. Our preliminary analysis at 3 years would suggest there is no difference in change in cognitive performance between the two groups and that there is a mild decline seen between 1 and 3 years that is most likely caused by a combination of normal aging and a progression of underlying cerebrovascular disease.

Multidisciplinary translational research is the cornerstone to reducing neurologic injury in patients undergoing cardiac surgery. Targeted therapies and emerging imaging technology will help to reduce this injury. Further work in the laboratory with its eventual translation to the patient's bedside will lead to improved care of our cardiac surgical patients. Ultimately gene screening will be able to identify those patients at greater risk and allow specific interventional strategies to be used in this high risk group of patients.

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# ANATOMY OF THE MITRAL VALVE

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## **General**

The valvar complex comprises the annulus, the leaflets, the tendinous cords, and the papillary muscles. Also important for its functioning is the left atrial musculature inserting to the leaflets and the myocardium to which the papillary muscles are inserted. The valve is obliquely located in the heart and has a close relation to the aortic valve. Unlike the tricuspid valve which is separated by muscle from its counterpart, the pulmonary valve, the mitral valve is immediately adjacent to the aortic valve.

## **Anatomy**

## **Mitral**

The annulus marking the hinge line of the valvar leaflets is more D shaped than the circular shape portrayed by prosthetic valves. The straight border accommodates the aortic valve allowing the latter to be wedged between the ventricular septum and the mitral valve. In this region, the aortic valve is in fibrous continuity with one of the two leaflets of the mitral valve. Expansions of fibrous tissues at either extreme of the area of continuity form the right and left fibrous trigones. The atrioventricular conduction bundle passes through the right fibrous trigone.

## **annulus**

Although the term annulus implies a solid ring-like fibrous cord to which the leaflets are attached, this is far from the case. In the area of aortic–mitral fibrous continuity, the distal margin of atrial myocardium over the leaflet defines the hinge line. When viewed from the ventricular aspect, however, the hinge line is indistinct since the fibrous continuity is an extensive sheet. There are prongs of fibrous tissues from each of the fibrous trigones but these were not continuous around the orifice. The annulus opposite the area of valvar fibrous continuity tends to be "weaker" in terms of lacking a well formed fibrous cord. This is the area affected in "annular dilation" and also most often involved in calcification of the annulus. With severe dilation, the minor axis of the valvar orifice becomes so distended that the leaflets, which are of fixed lengths, become unable to approximate each other.

## **Leaflets**

Distinctly different from the tricuspid valve, the mitral valve has two leaflets. These are notably different in shape and circumferential length. Owing to the oblique location of the valve, strictly speaking, its two leaflets do not occupy anterior/posterior positions nor is one of the leaflets "septal". The septal leaflet is characteristic of the tricuspid valve whereas neither of the mitral leaflets is attached to the septum. The corresponding terms for anterior and posterior are "aortic" and "mural". It is the aortic leaflet that is in fibrous continuity with the aortic valve. The aortic leaflet has a rounded free edge and occupies a third of the annular circumference, whereas the other leaflet is long and narrow, lining the remainder of the circumference. The aortic leaflet hangs like a curtain between the left ventricular inflow and outflow tracts. When the valve is closed, this leaflet appears to form the greater part of the atrial floor but is approximately equal in area to the mural leaflet. It meets the mural leaflet to form an arc shaped closure line, or zone of apposition, that is obliquely situated relative to the orthogonal planes of the body. With the leaflets meeting, the view of the valve from the atrium resembles a smile. Each end of the closure line is referred to as a commissure. These are designated the anterolateral and posteromedial commissures. It is worth noting, however, that the indentations between leaflets do not reach the annulus but end about 5 mm short in the adult heart. Therefore, there are no clear cut divisions between the two leaflets. Furthermore, the free edge of the mural leaflet is often divided into three or more scallops or segments described as lateral, middle, and medial or assigned terms like P1, P2, and P3. Although three scallops are most common, the scallops are not equal in size. The middle scallop tends to be larger in the majority of hearts. When the mural leaflet is deformed in a floppy valve, the middle scallop is likely to be prolapsed.

Normally, the valvar leaflets are thin, pliable, translucent, and soft. Each leaflet has an atrial and a ventricular surface. When viewed in profile, two zones can be distinguished in the aortic leaflets and three zones in the mural leaflet according to the insertions of the tendinous cords. In both leaflets, there is a clear zone that is devoid of chordal attachments. Nearer the free edge, the atrial surface is irregular with nodular thickenings. This is also the thickest part, corresponding with the line of closure and the free margin. Tendinous cords attach to the underside of this area described as the leaflet's rough zone. The rough zone is broadest at the lowest portions of each leaflet but tapers toward the periphery, or commissure, of the closure line. The basal zone that is found only in the mural leaflet is the proximal area that has insertions of basal cords to its ventricular surface.

Being distant from the ventricular wall, the aortic leaflet does not have attachments to basal cords. In normal valve closure, the two leaflets meet each other snugly with the rough zone and free edge in

apposition but at an angle to the smooth zone.

When the closed valve is seen in profile, the major part of the closure line lies below the plane of the atrioventricular junction rising toward the commissures at the peripheral ends so that the atrial surface of the leaflets has a saddle-like configuration. Being tethered by the tensor apparatus, the line of coaptation in a normal valve does not extend above the level of the junction during ventricular systole.

### **Tendinous cords**

The tendinous cords are string-like structures that attach the ventricular surface or the free edge of the leaflets to the papillary muscles. Characteristically, the tricuspid valve has chordal attachments to the ventricular septum allowing it to be distinguished from the mitral valve on cross sectional echocardiography. The tendinous cords of the mitral valve are attached to two groups of papillary muscles or directly to the postero-inferior ventricular wall to form the tensor apparatus of the valve. Cords that arise from the apices of the papillary muscles attach to both aortic and mural leaflets of the valve. Since cords usually branch distal to their muscular origins, there are five times as many cords attached to the leaflets as to the papillary muscles.

There are numerous classifications of tendinous cords. The predominant surgical classification distinguishes three orders of tendinous cord according to the site of attachment to the leaflets. The first order cords are those inserted on the free edge. They are numerous, delicate, and often form networks near the edge. Second order cords insert on the ventricular surface of the leaflets beyond the free edge, forming the rough zone. These are thicker than first order cords. Third order cords attach only to the mural leaflet since they arise directly from the ventricular wall or from small trabeculations. They insert to the basal portion of the leaflet and run only a short distance toward the free margin. In this area, webs may be seen in place of cords.

### **Papillary muscles and left ventricular wall**

Papillary muscles are the muscular components of the mitral apparatus. As a functional unit, the papillary muscle includes a portion of the adjacent left ventricular wall. Tendinous cords arise from the tips of the papillary muscles. Alterations in the size and shape of the left ventricle can distort the locations of the papillary muscles, resulting in valvar function being disturbed. The papillary muscles normally arise from the apical and middle thirds of the left ventricular wall. Described in most textbooks as two in number, however, there are usually groups of papillary muscles arranged fairly close together. At their bases, the muscles sometimes fuse or have bridges of muscular or fibrous continuity before attaching to the ventricular wall. Extreme fusion results in parachute malformation with potential for valvar stenosis.

Viewed from the atrial aspect, the two groups are located beneath the commissures, occupying anterolateral and posteromedial positions. A single anterolateral papillary muscle occurs in 70% of cases and in 60% of cases that there are two or three papillary muscles, or one muscle with two or three heads, in the posteromedial location. Generally larger than the posteromedial muscle, the anterolateral muscle is supplied by an artery derived from the circumflex or anterior descending branch of the left coronary artery. Since most people have right dominance of the coronary pattern, it is the right coronary artery that most often supplies the posteromedial papillary muscle.

Rupture of a papillary muscle is usually the consequence of infarction of the adjoining ventricular wall. If rupture involves the entire papillary muscle or its group, there will be torrential regurgitation since approximately half the support of each leaflet will be lost. Rupture confined to one head of the papillary muscle complex will be similar to breaking a major cord. During systole, the affected free edge fails to meet with the other leaflet and moves into the left atrial cavity.

### **SECTIONAL ANATOMY OF THE MITRAL VALVE**

Since the mitral valve is a complex with a unique arrangement of its component parts within the left ventricle, cross sectional imaging techniques including four dimensional echocardiography allow it to be visualised in its entirety by building up whole series of planes. The valve can be demonstrated in each of the orthogonal planes of the left ventricle, as well as in the orthogonal planes of the body.

Short axis planes through the ventricle display from apex to the cardiac base the oblique arrangement of the two groups of papillary muscles, the tendinous cords, the fish mouth appearance of the valvar opening, and the aortic outflow tract sandwiched between the ventricular septum and the mitral leaflet. This view allows assessment of the area of the valvar orifice. At right angles to the short axis plane, the long axis plane such as that obtained from the parasternal window produces the so-called two chamber plane. In this view, the mode of closure of the leaflets and the level of the closure line relative to the atrioventricular junction is seen to best advantage. The aortic and mural leaflets are readily distinguished, allowing detection of hooding, overshoot, or prolapse of each leaflet. The normal valve in closed position shows the aortic

leaflet at an angle to the long axis of the ventricle but the mural leaflet is perpendicular. It should be noted that in some normal valves the leaflets may balloon slightly past the plane of the atrioventricular junction during systole, but the zone of coaptation remains below the plane. In valvar opening, the mural leaflet becomes nearly parallel to the inferior wall while the aortic leaflet parallels the ventricular septum.

The second series of long axis sections through the left ventricle, the so-called four and five chamber planes, allow distinction between tricuspid and mitral valves. Being more or less parallel to the zone of apposition between leaflets, it is poor for detecting problems of coaptation. The series of two chamber sections obtainable from the apical window cuts the leaflets obliquely, distorting the true leaflet length and motion. Views of the mitral valve through the transgastric and transoesophageal windows enable more detailed studies of the entire length of the zone of apposition, revealing the arrangement of chordal supports at all segments of the leaflets.

# MITRAL VALVE DISEASE: AETIOLOGY OF DISEASE AND DEFINITIONS

Dr. R. Steeds – Queen Elizabeth Hospital, Birmingham.

## ASSESSMENT OF MITRAL VALVE DISEASE.

This lecture will provide an overview of the requirements for assessment of the patient leading to mitral valve surgery. Images will be shown to support the contention that echocardiography is fundamental to the correct identification of the aetiology of mitral regurgitation, severity, consequences for left ventricular function and suitability for repair. A summary of the relative benefits of the different imaging modalities will be given, together with a description of the potential of newer techniques for assessment.

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# MITRAL VALVE STENOSIS – WHO, WHEN AND WHY?

## The evidence base for intervention

### The choice of prosthesis and the influence of atrial fibrillation

**Mr. S. Kendall – James Cook University Hospital, Middlesborough.**

Isolated MS (male : female 1:2) occurs in 40% of all patients presenting with rheumatic fever (RF), and 60% of patients with MS have a history of RF. The normal valve area is 4 – 5 cm<sup>2</sup> and symptoms occur when the area is <2.5 cm<sup>2</sup>. Symptoms occur at rest when the area is <1.5 cm<sup>2</sup>. The transmitral gradient is related to the square of the flow and the diastolic filling period, so that symptoms are worse during exercise, emotional stress, infection, pregnancy and fast atrial fibrillation.

There is a 20-40 year latent period from the occurrence of RF until symptoms develop, and a further 10 years until the symptoms are disabling. When symptoms are minimal the 10 year survival 80%, (60% have no progression), but when symptoms occur at rest the survival becomes dismal at 0-15%. If MS is untreated death is caused by heart failure (60-70%), systolic embolus (20-30%) and pulmonary embolus (10%). MS rarely causes sudden death.

At presentation always exclude differential diagnoses such as atrial myxoma, cor triatum and parachute mitral valve.

The investigation and assessment of MS are covered by Dr Steeds' presentation.

**Mild MS.** (Area >1.5 cm<sup>2</sup> and mean gradient <5mmHg).

Asymptomatic : observe with routine follow up and echo assessment.

Symptomatic: counsel regarding precipitating factors and prescribe B blockers to maintain sinus rhythm and prevent tachycardia. Consider intervention if systolic pulmonary artery pressure >50mmHg; ie with balloon valvotomy, valve repair, but probably not the time for MVR.

30-40% of patients develop **Atrial Fibrillation**. Warfarin gives 4-15 fold reduction of systemic / pulmonary emboli. 10-20% of patients will have systemic emboli, 33% of events within 1 month of onset of AF and 66% within 1 year. The recurrence rate of emboli is high and the overall risk is related to age but **not** to the severity of the MS nor the size of the atrium.

*? Will this become the time for mitral surgery and maze procedure?*

**Moderate to severe stenosis.** (Moderate: area <1.5 cm<sup>2</sup> and mean gradient >5mmHg, severe <1.0 cm<sup>2</sup> and mean gradient >15mmHg). Patients in NYHA III / IV are all referred for intervention as their prognosis is poor – preferably before class IV symptoms develop as their risk from surgery is greater and the benefits are less. Patients with severe MS are rarely asymptomatic, but should still be considered for intervention.

**Open Commissurotomy.** Operative risk of 1-3% and a 5 year reoperation rate of 5-7%. The 5year complication free survival is 80-90%.

**Balloon valvotomy.** Developed in the eighties and approved in 1994. Needs favourable anatomy and absence of thrombus. 80-95% of patients have a 'successful' procedure (mortality 1%) and it usually doubles the valve area, 60% obtain a reduction in gradient, 2-10% get severe MR and <12% get a significant ASD. The event free survival is 50-65%.

**Mitral Valve Replacement.** At present MVR is for: patients unsuitable for valvotomy; combined stenosis / regurgitation; functional class III and IV patients; patients post-valvotomy. The risk of surgery is dependant on functional status, age and left ventricular function. The overall peri-operative mortality risk is 4.5% and usually gives very good symptomatic relief.

Choice of Prosthesis ( ie risks of warfarin versus re-operation). Reports are varied in complication rates ie in one study the annual risk of embolism and / or complications of anti-coagulation in elderly patients (>65 years) was 0.36% for tissue valves (n=326) and 1.08% for mechanical valves (n=250), with 7 re-operations in the tissue group and 2 in the mechanical group. The risk of redo MVR is 4.7% compared to 4.1% first time, and pericardial valves now have <15% risk of failure by 15n years. A meta analysis of the INR in patients with mechanical MVR shows that an INR >3 decreases the risk of thromboembolism significantly more than the increased risk of bleeding.

The risk of embolic stroke is increased in patients >75 years, female, continued smoking, presence of atrial fibrillation and impaired left ventricular function.

The long term benefits of concomitant maze procedure is yet to be evaluated, but early results

show restoration of sinus rhythm in 70-80% in patients with persistent AF, and 90-95% restoration in recent onset or paroxysmal AF.

In summary, a pericardial mitral valve replacement has good durability, and should possibly be combined with a Maze procedure (includes stapling of the left atrial appendage). This decreases the risk of thromboembolism and decreases the need for a high INR. However, the mechanical mitral valve has excellent durability and the risks of warfarin are still small, even to the foetus during pregnancy.

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# **WHEN TO OPERATE IN PATIENTS WITH MITRAL REGURGITATION**

**Mr. M. Underwood – Bristol Royal Infirmary.**

The benefits of mitral valve surgery in patients with severe symptomatic mitral regurgitation are well established and result in improvements in symptomatic status and long-term survival. Less well defined are the indications for surgery in patients with severe regurgitation but minimal or no symptoms. Historically, in this patient group, surgery has been deferred until there is evidence of worsening symptoms or left ventricular dilatation. This philosophy has been adopted because mitral valve replacement may have deleterious effects on left ventricular function and the insertion of a prosthetic valve has its own morbidity in terms of warfarinisation, thromboembolism and endocarditis. Also, it has been thought that many patients with minimal or no symptoms may not show a definite deterioration if treated medically. Surgical and cardiological philosophy regarding this patient group has changed in recent years mainly due to data from the Mayo clinic defining the unsatisfactory clinical deterioration in these patients if medically treated in conventional fashion and the fact that now mitral repair techniques are well established, these patients can undergo surgery and not be subjected to the subsequent morbidity of having a prosthesis inserted. Surgery for this patient group is now being advocated at an early stage in the disease process with data demonstrating that this philosophy, in the hands of surgeons with experience of mitral valve repair, may well result in better outcomes in terms of long term survival and also a higher proportion of valve repair vs replacement if operative intervention is instituted early .

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# **PRINCIPLES IN RESTORATION OF MITRAL VALVE COMPETENCE**

**Dr. P. Perier - Herz und Gefäß Klinik, Bad Neustadt/ Saale, Germany.**

Mitral valve repair is nowadays a recognized method to surgically treat mitral valve regurgitation. Alain Carpentier has during the past twenty years has worked on the improvement of the surgical techniques, one of the milestones of his work has been the “ functional approach ”<sup>i</sup>.

Another major breakthrough has been the onset of echocardiography whose role before, during and after the operation has grown to a point where echocardiographers should form tight teams with surgeons. The contributions of echocardiography in mitral valve repair are numerous: for the timing of surgery, for the precise description of the lesions for a preoperative recognition of the etiology, in recognizing intraoperative complications, left ventricular outflow tract obstruction or residual regurgitation, for the follow-up of the patients etc....

Basically, mitral valve regurgitation can be defined as a loss of an efficient surface of coaptation during systole. The aim of mitral valve repair is to restore a good surface of coaptation, thus restoring a competency to the mitral valve.

Mitral valve repair require specific surgical training and skills even in what can be considered the most usual and simple lesion, the prolapse of the posterior leaflet whose standardized treatment is quadrangular resection and plication of the annulus. Nevertheless in many instances other techniques, more sophisticated are required<sup>ii</sup>. These difficulties may explain the low rate of 35% of repair in comparison with replacement in Europe.

Mitral valve repair has been shown to be as efficient for anterior leaflet prolapse<sup>iii</sup>. There is today little doubt that long time survival after surgery for mitral valve regurgitation is better after mitral valve repair than after mitral valve replacement. Two groups of patients operated in our institution with mitral valve regurgitation were compared<sup>iv</sup>. One group (433 patients) had mitral valve repair and the other (257 patients) mitral valve replacement with Medtronic-Hall prosthesis. The 7-year survival was 74% for the repair group and 58% for the replacement group. This difference was statistically significant. The same differences were observed in subgroups of patients having either isolated mitral valve regurgitation or associated with CABG. It is interesting to note that at 7 years, the reoperation rate was 5% for the repair group and 9% for the replacement group. This underlines the durability and the stability of the repair techniques. The durability over time is dependant of the etiology of the mitral disease as demonstrated by Carpentier's team<sup>v</sup>. A study recently published by this group showed at 25 years a 7% reoperation for the group of degenerative disease and an incidence of 53% of reoperation for the group of rheumatic disease<sup>vi</sup>. The trend nowadays<sup>vii</sup> is to operate patients with severe mitral valve regurgitation at an early stage when they are not yet symptomatic the goal being to preserve the left ventricular function that might deteriorate unnoticed. Two groups of patients with isolated mitral valve regurgitation have been compared. Seventy-nine patients were non-symptomatic and one hundred eighty four symptomatic. The 7-year survival was 95% for the non-symptomatic group and 75% for the symptomatic group.

In conclusion, improvements in surgical techniques, a better understanding in particular with the help of echocardiography have given mitral valve repair safety, predictability, and durability. Mitral valve repair can be proposed to non-symptomatic to prevent left ventricular dysfunction.

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# **ISCHAEMIC MITRAL VALVE REGURGITATION – SURGICAL TREATMENT AND ADJUVANT THERAPIES**

**Mr. B. Bridgewater – Wythenshawe Hospital, Manchester.**

Ischaemic heart disease can cause mitral regurgitation (MR) in several ways – acute myocardial infarction, which will not be considered here, can cause acute papillary muscle rupture or dysfunction and MR. Chronic ischaemic heart disease can lead to myocardial infarction that can in turn cause MR. The mechanisms of MR in this setting is dysfunction and distortion of left ventricular myocardium and papillary muscles, which may lead to tethering, usually of the posterior leaflet of the mitral valve which may be further compounded by failure of systolic contraction of the mitral annulus. Ischaemic cardiomyopathy may cause a spectrum of symptoms including angina, heart failure and a combination of the two. Analysing the data is made more complex as some trials have been performed for patients purely with angina, others purely for heart failure.

Mitral regurgitation in this setting may be clinically silent with little or no audible murmur and its significance is often underestimated by echo – significant regurgitation for degenerative MR is defined by a regurgitant volume of greater than 45 mls, but in ischaemic MR a regurgitant volume of greater than 30 mls is thought significant. MR is common in patients with impaired LV function, and isolated CABG alone does not improve moderate or severe MR in most cases<sup>1</sup>. The severity of CABG is underestimated by TOE at the time of surgery, unless provocative tests are used. Leaving patients with residual MR after coronary artery surgery adversely affects life expectancy<sup>2,3</sup> – this is not just an effect of MR being a marker of more severe LV dysfunction – mild to moderate residual MR is an independent predictor of poor prognosis.

There is mixed data on whether mitral repair at the time of CABG improves prognosis in patients with moderate to MR and angina,<sup>4,5,6,7,8</sup>. On balance the data suggests survival is better, and that symptoms are better controlled if the mitral valve is repaired.

There is evidence that some additional treatments may help improve prognosis in patients with poor LV function. Implantable cardiac defibrillators improve outcome in this group<sup>9</sup>, and this applies to patients who have also undergone CABG. Cardiac resynchronization therapy (biventricular pacing) improves MR in patients with poor LV function<sup>11</sup> and for patients with symptoms of heart failure combined treatment with ICDs and resynchronisation therapy improves outcome<sup>12</sup>.

Patients with poor LV function and MR due to ischaemic heart disease are a difficult group to treat with bad longterm outlook. Surgery with revascularization and mitral repair improves outcome, but many of these patients have high degrees of predicted operative risk. Some of these patients will also benefit from ICD +/- resynchronisation therapy. Some may benefit from these therapies instead of surgery. Optimal treatment strategies are best defined by a team approach include surgeon and cardiologist with expertise in EP treatments.

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# **SURGERY FOR TRICUSPID VALVE REGURGITATION**

**Dr. P. Perier - Herz und Gefäß Klinik, Bad Neustadt/ Saale, Germany.**

The tricuspid valve remains an enigma and tricuspid valve dysfunctions are too often ignored and untreated.

Most of the time, tricuspid regurgitation is a finding in patients with advanced mitral valve disease. The tricuspid regurgitation is functional secondary to pulmonary hypertension and right ventricular dilatation leading to a dilatation of the tricuspid annulus. Patients that require a simultaneous tricuspid valve surgery have to be clearly identified, which remains a difficult task. There are no clear parameters to help for the decision making. It seems that nowadays the most reliable criteria is the dilatation of the annulus as measured by echocardiography or during the surgical exploration . Many surgical techniques have been described to narrow the dilated tricuspid annulus, sutures, commissuroplasty etc... the basic principle of the Carpentier annuloplasty ring is to reshape and to restore normal proportions to the various components of the tricuspid valve. All the technical refinements of valve reconstructive surgery may be needed to reconstruct a good surface of coaptation, and the new developments, artificial chordae; pericardial substitutes have considerably reduced the indications for tricuspid valve replacement.

More rarely tricuspid valve disease is isolated as can be seen in congenital malformation, after bacterial endocarditis or traumatism.

Valve repair is the technique of choice to surgically treat dysfunctions of the tricuspid valve. The prognosis is totally different if the tricuspid valve disease is isolated or associated with left-sided valve dysfunctions being then the consequence of right ventricular dysfunction. Echocardiography is the method of choice to study the tricuspid valve and to select the patients who require tricuspid surgery.

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## **CARDIOPULMONARY BYPASS**

**Mr. I. Wilson, Mr. R. Gohil, and Dr. D. Green, Dr. P. Townsend -  
Queen Elizabeth Hospital, Birmingham.**

These seminars will explore some of the following scenarios. These sessions will be of a practical/interactive nature. The aim is to develop recognition/management of potentially life threatening problems which may occur during cardiopulmonary bypass including:

WEANING FROM CARDIOPULMONARY BYPASS

AIR EMBOLISM

CANNULATION PROBLEMS

EXCESSIVE ARTERIAL LINE PRESSURES

LOW PO<sub>2</sub> LEVELS ON CPBP

USE OF APROTININ/CONTROL OF ACT

POOR VENOUS RETURN/AIR LOCK

PROTAMINE ANAPHYLAXIS

USE OF CENTRIFUGAL PUMPS

MANAGEMENT OF IVC TEAR DURING CPBP

OXYGENATOR FAILURE

### **Suggested Reading**

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