



# **FUNCTIONAL ANATOMY OF THE AORTIC VALVE**

**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-valvar and sub-valvar components. The supra-valvar components, in essence, are the aortic sinuses, but they contain at their base structures of ventricular origin. The supporting sub-valvar parts are primarily ventricular, but extend as three triangles to the level of the sinutubular junction. Stenosis at the level of the sinutubular junction is usually described as being "supra-valvar". 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 sinutubular 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.



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## NOTES

# **AORTIC STENOSIS - THE EVIDENCE BASE FOR SURGERY**

## **WHO, WHY, WHEN. The Influence of Coronary Artery Disease**

**Mr. M. Dalrymple-Hay - Derriford Hospital, Plymouth.**

### **Aims:**

Discuss AHA/ACC guidelines for AVR

Differentiate indications for AVR in asymptomatic patients.

Discuss factors associated with worse prognosis in asymptomatic AS

Understand rationale AVR in patients undergoing CABG

Understand issues low aortic valve gradient and poor LV function

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## NOTES

## **AORTIC VALVE REPLACEMENT**

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

Two randomized prospective trials of biological vs mechanical prosthesis established the concept of balancing the structural deterioration of biological valves over time with the risks of associated anticoagulation with mechanical valves when choosing the most appropriate prosthesis for an individual patient. The results of multiple cohort investigations have re-enforced this concept and conventional interpretation of the overall data suggests mechanical valves are most suited to patients under the age of 65 years and biological valves otherwise. However, a rational decision must be individualized for each patient and take into account their life expectancy, associated co-morbidity, contra-indications to anticoagulation and personal preference. For example, the 10 year survival of a patient with aortic valve disease maybe reduced from 70% to 40% if there is associated coronary artery disease. Proponents of biological valves point to evidence of greater durability of the 'modern' day prosthesis and the reducing risks of any subsequent re-intervention when making a case to expand their use. Proponents of mechanical valves point to their well established durability and the reducing risks of associated anti-coagulation problems with modern regimes and alternative therapies. For stentless bioprosthesis, randomized clinical studies comparing them to stented valves have produced differing outcomes and disagreement as regards improved outcomes. There is little definitive evidence of superiority, particularly in patients with small aortic root diameters. Likewise, when considering the risks of patient-prosthetic mismatch there is conflicting data but little compelling evidence that it exists as an important clinical problem in contemporary cardiac surgical practice.

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## NOTES

# **PATIENT PROSTHESIS MISMATCH IN AORTIC VALVE**

## **REPLACEMENT: POSSIBLE BUT PERTINENT?**

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

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 bedevilled 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 labelled 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 labelled 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 co morbid 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 that PPM as defined in their paper as  $<1.2\text{cm}^2/\text{m}^2$ , was rare. There was a small increase in in-hospital mortality 1-2%, although intermediate and long-term mortality were unchanged when compared to the PPM group.



### **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 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, 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 manoeuvres 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.



# **AORTIC REGURGITATION, AORTIC VALVE REPAIR AND**

## **AORTIC ROOT PRESERVATION TECHNIQUES**

**Professor M. Redmond - Our Lady's Hospital, Dublin.**

AHA and ESC guidelines recommend corrective surgery for severe aortic regurgitation (AR) in symptomatic patients (recommendation class/level of evidence, I/B), in asymptomatic pts with resting LVEF  $\leq 50\%$  (I/B), in asymptomatic pts with LVEF  $> 50\%$  with LVED dimension  $> 70\text{mm}$  or LVESD  $> 50\text{mm}$  (IIa/C); in pts undergoing CABG, ascending aortic or other valve surgery (I/C). Corrective surgery for any degree of AR is indicated for pts with aortic diameter  $\geq 45\text{mm}$  for Marfan pts (I/C);  $\geq 50\text{mm}$  for bicuspid valve pts (IIa/C) and  $\geq 55\text{mm}$  for other pts (IIa/C).

Experience is growing with aortic valve repair for cusp prolapse, perforation, retraction/thickening and commissural disruption along with uni- and bicuspid aortic valves, rendering these techniques realistic alternatives to aortic valve replacement (AVR), especially in young pts and in pts undergoing aortic root repair.

Aortic root preservation techniques including remodeling, reimplantation and tailoring (sinotubular reconstruction) have evolved over time and the modified versions now demonstrate good mid-term durability. The Sinus of Valsalva graft for root reimplantation has proved to be easy to use and versatile with  $90.8\% \pm 3.3\%$  freedom from AVR at 5yrs. It appears to be particularly effective in preventing postoperative annular dilatation in pts with connective tissue disorders.

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# **MINIMALLY INVASIVE VEIN HARVESTING**

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# RECENT EVIDENCE ON THE VALUE OF CAROTID SURGERY PRIOR TO CORONARY SURGERY

**Professor J. Dark, - Freeman Hospital, Newcastle upon Tyne.**

Much of the background to this debate springs from the 2004 AHA Guidelines<sup>1</sup>, which very firmly advocate pre-operative carotid endarterectomy (CAE) as being a “proven” manoeuvre to reduce the risk of post-operative stroke. This conclusion is reached by examining the risk of stroke with known carotid disease, quoting papers from 12 and 14 years ago. Risks are said to range from 10% when stenoses are between 50 and 80% , and 11% to 18.8% with stenoses greater than 80%. If there is bilateral severe disease, or an occlusion with severe contralateral stenosis, the risk is 20%. This last observation comes from 1984. The numbers in these studies are small. On the other hand, there are three separate studies quoted showing that CAE done pre-operatively can have a stroke rate of less than 4% and a mortality rate of 3%. Ergo it must be safer than doing nothing!

The same guidelines also recommend epi-aortic echo to detect mobile plaque. They state that 1 in 3 strokes are probably related to aortic plaque, and echo, with subsequent manoeuvres to reduce aortic manipulation, has been shown to reduce stroke rate.

They identify post-op AF as increasing the stroke rate by a factor of 2-3, and recommend anticoagulation with heparin and then warfarin for AF that persists for more than 24 hours.

**Few centres in the UK routinely do either epi-aortic echo or early anticoagulation for AF, despite these being recommendations from the AHA.**

Finally, they document the increase of stroke risk with age, suggesting the risk is 2-6% at 70, and between 8 and 10% at 80.

All of these risk factors, and indeed much of the literature, is from papers 10-20 years old. The stroke rate in Newcastle 20 years ago, from Pam Shaw’s 1985 study, was 5%. She studied a group of 312 patients, but the mean age was 53.4 and the oldest was just 70. Our rate last year was 1.9%, admittedly from the PATS database, but with a much older mean age of 67.

Relatively little has been published since the AHA document, but there is very good, critical analysis of the literature from Prof Ross Naylor, a vascular surgeon in Leicester. He has done a number of detailed systematic reviews<sup>2,3</sup>. The conclusions are best summarised in his 2004 paper. Although carotid disease is clearly an important aetiological factor, there is little published data on the risk of *ipsilateral* stroke in a screened patient with disease who undergoes CABG alone. It is likely that carotid disease is responsible for no more than 40% of strokes. On the other hand, from the literature, 9-11% of patients who undergo a staged or synchronous procedure will die, have a stroke or an MI. Naylor states “***Because of the paucity of natural history data no systematic evidence exists that staged or synchronous operations confer any benefit over CABG alone.***” If a procedure is done, there is some evidence to suggest that staged, ie CAE followed by CABG is safer than synchronous procedures are safer, although this may just represent a trend to select the sickest patients for combined operations.

There are two more recent publications worth noting. Dubinsky and Lai analysed the risk of CEA plus CABG compared with CABG alone, from a large database – the US Nationwide Inpatient Sample<sup>4</sup>. They had data on about 180,000 CAE patients and just under 500,000 CABG’s, with risk-stratification data on both groups. Between them, there were 1230 done on the same day and almost 6000 on the same admission. The Odds Ratio for death or stroke was more than 2.0 for all the combined procedures – this is not surprising, given the high risk nature of patients needing two procedures. It was the same whether on the same day or same admission.

But after controlling for all the risk factors, the odds ratio was still 1.38, which for a population of this size,



is a very significant risk. Whilst the methodology may be flawed, the numbers are huge, and the paper was accepted by a major journal. The conclusion was that a randomised study is required.

In the real world, there is a fascinating small study from Sheffield<sup>5</sup>. It comes from a group of neurologists and neuro-radiologists who work with cardiac surgeons, some of whom demanded intervention for carotid disease pre- CABG. Since 1998 they have had a policy of carotid stenting in this setting, and report on 52 patients who had this intervention. Criteria for stenting were rigorous - >80% stenosis on the dominant hemisphere, >150% combined stenosis, symptomatic stenosis>70% or an occlusion with contralateral stenosis >50%. There were no strokes related to stenting. Three patients died before surgery, despite no patient waiting more than 2 months. There were 3 non-fatal and 2 fatal strokes, together with one other cardiac death, in the 30 days post surgery. All the non-fatal strokes were ipsilateral to the stent.

In this small group of patients, there was a combined major stroke, minor stroke and death rate of 19%! All of the complications were due either to surgery or delay in surgery, and there was an 8% ipsilateral stroke rate despite stenting!. The authors again suggest this can only be resolved with a multicentre trial.

There is no doubt about the situation with regard to *symptomatic* patients; urgent treatment is required. The benefit from surgery is greatest is within the first two weeks of an ischaemic event. In the trials of symptomatic patients, five patients were required to undergo CEA to prevent one stroke in the first two weeks. The figure for patients treated after 12 weeks was 125 patients!<sup>6</sup>

The patient without neurological symptoms with planned cardiac surgery represents a conundrum. Surgery may be delayed because of a perceived need to investigate asymptomatic patients. If carotid disease is found there is then the question of what to do about it. The various large studies of asymptomatic patients have established a role for endarterectomy (but not yet for stenting) in preventing a stroke over a 5 *year* time period. There is about a 3% chance of stroke or death in these patients if there is no cardiac disease, so it is probably higher in our patients. In a recent review of largely asymptomatic patients referred for carotid stenting prior to CABG there was 4.7% incidence of death or stroke associated with the stent alone, and a combined death and stroke rate of 12.3% for the two operations!<sup>7</sup> These authors yet again suggested the need for a trial

**There is no good evidence that any intervention on the carotids will reduce the peri-operative risk of stroke for cardiac surgery.**



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**ANTIFIBRINOLYTICS**

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**PEROPERATIVE GRAFT FLOW & PATENCY**

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# **CORONARY ARTERY BYPASS GRAFT VERSUS PERCUTANEOUS**

## **CORONARY ANGIOPLASTY: CABG ON THE REBOUND?**

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**Purpose of Review** To examine the benefits of coronary artery bypass grafting (CABG) against percutaneous coronary intervention (PCI) and particularly the use of drug eluting stents (DES) in situations where CABG has traditionally been considered the most effective therapy on clinical and economic grounds.

**Recent Findings** Current studies reconfirm that CABG is still the best therapy in terms of improved survival and freedom from reintervention for most patients with proximal left anterior descending, multivessel and left main coronary artery disease (CAD) and that these benefits are even greater in diabetic patients. Health economic analyses also confirm the cost effectiveness of medical therapy and CABG but not PCI. Furthermore, several metaanalyses have shown that DES do not improve survival or freedom from myocardial infarction over bare metal stents but increase the risk of stent thrombosis with its associated medical and financial implications for prolonged dual antiplatelet medication.

**Implications of the findings for clinical practice** In view of the evidence in favour of CABG this article questions the justifiability of some trials of PCI vs CABG, especially in diabetic patients and those with left main stem CAD, and exhorts the need for a multidisciplinary team approach to the management of CAD as a 'minimum standard of care'.

**KEY WORDS:** coronary artery bypass grafting (CABG); percutaneous coronary intervention (PCI); multivessel and left main coronary artery disease; cost effectiveness; drug eluting stents; diabetes; multidisciplinary team.

### **Introduction**

The last decade has witnessed the relentless growth of percutaneous coronary intervention (PCI) in patients with stable coronary artery disease (CAD). In many industrialised countries the ratio of PCI to CABG now exceeds 4 to 1 [1]. The initial promise, however, that drug eluting stents (DES) would eliminate the problem of restenosis has proved not to be the case, particularly with more complex lesions, and is compounded by an increased incidence of early and late stent thrombosis particularly when used in off label settings [2\*]. In view of continuing mortality and high repeat rates of revascularization with PCI best evidence suggests that coronary artery bypass grafting (CABG) is still the best therapy for most patients with multi vessel and left main CAD both on clinical and economic grounds.

### **Isolated left anterior descending coronary artery**

The left anterior descending coronary supplies a greater amount of myocardium than the circumflex or right coronary arteries and, consequently, disease in its proximal portion has more important adverse prognostic significance even in asymptomatic patients when there is objective evidence of ischaemia [3]. The most durable and proven treatment is revascularization with an internal mammary artery (IMA) graft which significantly reduces the subsequent risk of death, myocardial, recurrent angina and any need for further intervention [4,5]. The conventional requirement for a median sternotomy incision and cardiopulmonary bypass has, nevertheless, resulted in the less invasive option of PCI with stents increasingly replacing CABG, unless contraindicated by anatomical (eg ostial lesion) or pathological complexities.

However, a recent meta-analysis has demonstrated that an IMA graft to the left anterior descending coronary artery by a minimally invasive approach on the beating heart is both clinically [6\*\*] and economically [7\*\*] more effective than stenting with bare metal stents (BMS) over a four year follow-up period. PCI resulted in a three fold increase (13%) in recurrent angina and the need for reintervention in comparison to surgery (4%) [6\*\*]. Although there was no difference in survival between the interventions it



is possible that a potential survival benefit of surgery was underestimated both because of the relatively limited duration of follow up and because more severe and complex lesions, unsuitable for stenting, would have been excluded from the trials but still have benefited from surgery. Consequently, while some patients with proximal left anterior descending CAD which is amenable to both interventions may favour the less invasive approach of PCI it is important that they understand that there is a substantially higher risk of reintervention, at least with BMS, and that they may be foregoing a survival advantage from an IMA graft.

### **Multi Vessel Coronary Artery Disease**

The use of PCI in multivessel CAD has been based on 15 randomised trials of PCI versus CABG which individually reported similar survival (but at least a three fold increase in repeat interventions) with PCI. However the results of these trials may be applicable to only small groups of patients with multivessel CAD as the trials only included around 5% of all potentially eligible patients, predominantly those with single or double vessel CAD and normal left ventricular function [8\*\*] a group who are known to have little prognostic benefit from CABG [4]. For example, in the 1829 patients in the BARI trial only 41% had three vessel CAD, only 36% had a significant LAD stenosis and around 80% had normal left ventricular function [9\*\*]. And the same type of patients largely dominated the more recent ARTS [10] and SoS [11\*\*] trials which involved the widespread use of stents. By largely excluding patients with more severe disease who have a proven survival benefit from surgery (ie three vessel CAD, chronic total occlusions and impaired left ventricular function) the trials were, in effect, not only biased against the prognostic benefit of CABG [8\*\*] but by being used to justify PCI in such patients have denied them the prognostic benefit of surgery.

Even so a meta-analysis of these trials, involving almost eight thousand patients followed for up to eight years, did show a small but prognostically significant benefit of CABG translating into an NNT of 53 and accompanied by a three fold reduction in need for repeat reintervention at five years [12]. While the ARTS trial found a similar five year survival of 92% between CABG and PCI in its 1205 patients [10] the SoS trial reported significantly better five year survival for CABG (93.4%) than PCI (89.1%) in its 988 patients [11\*\*].

However, it is important to emphasise again that these trials almost certainly underestimate the true survival advantage from CABG for two reasons: (i) analysis on an intention to treat basis discounts the benefits accrued by those PCI patients who cross to CABG eg 58% of BARI PCI patients had actually undergone CABG by 10 years [9\*\*]; (ii) as explained above these trials contained relatively low risk patients in whom the prognostic benefit of CABG is less definite.

As expected the greatest benefit from CABG was seen in those patients with more extensive CAD [12] and is consistent with the results from several large observational data bases which have consistently shown a survival benefit for CABG in patients with multivessel CAD [13-16]. For example in the New York Registry of almost 60,000 patients, propensity matched for cardiac and non-cardiac comorbidity, within 3 years of follow up there was an absolute 5% decrease in survival and a 7 fold increase in the need for reintervention in patients undergoing PCI in comparison to CABG [14]. Similar results were reported in the Cleveland Clinic [13] Northern New England [15] and Duke [16] databases.

### **Left Main Stem Stenosis**

LMS stenosis is reported to be present in 4%-6% of patients undergoing coronary angiography [17\*\*,18] and in up to 30% of CABG patients [19]. Because of its proven survival benefit CABG has generally been regarded as the “gold standard” therapy for significant left main stem (LMS) stenosis for the last decade in ACC/AHA guidelines for CABG [20] and in both ESC [21] and ACC/AHA [22,23] guidelines for PCI. However in a recent survey of interventions in patients with LMS stenosis, 29% of European patients and 18% of North American patients underwent PCI rather than CABG [24\*\*].

While the proximal anatomic position of the left main coronary artery and its relatively large diameter make it an attractive target for PCI two important factors mitigate against long-term success with PCI. First, up to 90% of stenoses are distal and/or bifurcating lesions [25-32\*\*] which are notoriously prone to restenosis [33-36] and, second, up to 80% of patients have concomitant multi-vessel CAD [25-32\*\*] where CABG already offers a survival advantage [13-16]. Serruy’s group emphasized the importance of distal LMS stenosis in predicting adverse outcomes reporting that after a median follow up of 20 months, in 130 patients with LMS stenosis, the cumulative incidence of major adverse cardiac events was 30% in



patients with distal versus 11% in those without distal disease ( $p=0.007$ ) mainly driven by the different rate of target vessel revascularization (13% vs 3%;  $p=0.02$ ) [36\*\*].

The relevance of PCI studies in LMS stenosis to real clinical practice is also frequently compromised by absence of precise data on selection criteria for PCI rather than CABG, the proportion of all LMS stenosis patients undergoing PCI rather than CABG, the proportion of PCI patients ineligible for CABG because of other co-morbidity (who were therefore also high risk for PCI) allied to incompleteness of angiographic follow-up and limited duration of clinical follow-up (rarely exceeding two years) which discounts the survival benefit of CABG which accrues with time.

Eight studies of BMS, conducted between 1999-2003, and involving over 1100 patients had an overall in-hospital mortality of 6% with a need for further immediate revascularisation averaging 4% (range from 0% to 20%) [8]. Most importantly however by two years of follow-up overall mortality averaged 17% (range 3% to 31%) and the need for repeat revascularisation rate averaged 29% (range 15% to 34%) [8]. Better results with BMS have been reported in younger patients with good left ventricular function, predominantly ostial or mid shaft LMS lesions and a lower incidence of concomitant CAD with mortality rates of 3.4% [37] to 7% [38] at one year and 7.4% [39] at three years but with respective repeat revascularization rate of 32%, 28% and 28%. It should, however, be borne in mind that the risks of CABG would also be low in such low-risk populations eg the one year mortality in 504 CABG patients in the SoS trial was 0.8% [11\*\*].

The ability of DES to reduce restenosis has encouraged their use in LMS stenosis [25-32\*\*] although, again, relevance to real clinical practice is also hampered by lack of detail regarding eligibility criteria for PCI vs CABG, small individual patient numbers (50 to 130 per study), incomplete angiographic assessment of restenosis and limited clinical follow-up (usually less than a year). However, as a higher proportion of these patients had distal or bifurcation LMS stenosis (up to 90%) and also significant CAD (up to 100%) early results appear encouraging with an average in-hospital mortality of 2% and an average immediate repeat revascularisation rate of 2%. However at a mean follow-up of less than a year (range 6-18 months) mortality had increased to 7% and repeat revascularisation to 13% (range from 2%-38%). In the only study with complete angiographic follow-up, at both three and then nine months, Price and colleagues reported that the restenosis rate increased from 34% to 44% [28\*\*]. Ominously, two of these studies cautioned that as restenosis is frequently asymptomatic surveillance angiography is mandatory [28\*\*,32\*\*]. It is uncertain, however, how often or for how long repeat angiography is necessary in this critical location and its associated financial implications.

Although several trials of PCI vs DES in LMS are ongoing, including the SYNTAX, FREEDOM and LEMANS no results have yet been formally reported Three registries have compared CABG and DES in patients with LMS stenosis [29,31,32\*\*]. In the Bologna Registry of 154 CABG and 157 PCI patients [32\*\*], at a median follow up of 14 months the overall respective mortality was 12% and 13% (but 3% respectively in low risk patients), with an eight fold increase in repeat revascularization with DES (26% vs 3%). In an Italian Registry [29] of 107 PCI and 142 CABG patients one year mortality was similar after adjustment for baseline characteristics but the need for repeat revascularization was 20% for PCI and 4% for CABG patients. Lee and colleagues reported six month outcome in 50 PCI and 123 CABG patients with LMS stenosis but the small numbers and short follow up make data difficult to interpret [31].

The UK Society of Cardiothoracic Surgery database reported 3% mortality in all five thousand patients undergoing CABG for LMS stenosis in 2003 in contrast to a mortality of 1.8% in all seventeen thousand patients without LMS stenosis [19]. Whether surgical results can be improved further with the use of off-pump CABG and composite arterial grafts based on bilateral IMA grafts [40], to simultaneously avoid the use of cardiopulmonary bypass and to permit a no-touch aortic technique (thereby reducing the risk of stroke), is the subject of ongoing trials [41\*].

## Diabetes

The BARI trial has recently confirmed that even in relatively low risk diabetic patients (only 50% had three vessel CAD, only 40% had true proximal LAD disease and most had normal ventricular function) there is a survival advantage at 10 years for CABG in comparison to PCI (58% vs 46%  $p=0.025$ ) [9\*\*]. This is also consistent with five year survival data for 208 diabetic patients in the ARTS trial (CABG 92% vs PCI 87%) [10] and 147 diabetic patients in the SoS Trial (CABG 94.6% vs PCI 82.4%) [11\*\*]. In addition to the survival advantage for CABG there was a striking difference in the need for overall reintervention in the



BARI trial (18% of CABG and 80% of PCI patients [9\*\*]) and in the 208 diabetic patients in the ARTS trial (10% of CABG and 43% of PCI patients [10\*\*]).

As indicated earlier the survival benefit for CABG may be greater in real life in diabetic patients with more severe CAD who were excluded from the trials. In a regional database of 7,159 diabetic patients who underwent coronary revascularization during 1992 to 1996, 2,766 (39%) were similar to those in the BARI trial. Of these, the 736 who underwent PCI were younger, had higher ejection fractions and less extensive coronary disease than the 2030 who underwent CABG but when adjusted for differences in baseline clinical characteristics, had a significantly higher overall mortality (HR = 1.49; p = 0.04) and particularly so in the 1,251 patients with 3VD (HR = 2.02; p = 0.04) [42].

### **Two reasons why CABG offers a survival advantage for multi vessel and left main CAD**

There are two reasons which probably explain the consistent survival benefit for CABG reported in several large observational studies [13-16]. First, because bypass grafts are placed to the mid coronary vessel, CABG protects whole zones of vulnerable proximal myocardium not only against the 'culprit' lesion (of any complexity) but also offers prophylaxis against new lesions in diffusely diseased endothelium. In contrast, PCI only treats immediate culprit lesion, assuming that it is technically feasible, but has no protective effect against the development of new proximal disease. Second, the failure of stenting to achieve complete revascularization in most patients with multivessel disease reduces survival proportional to the degree of incomplete revascularization [43\*\*]. Over 22000 patients from New York State's Percutaneous Coronary Interventions Reporting System were subdivided by complete (69%) or incomplete (30%) revascularization. After adjustment for baseline differences, patients with incomplete revascularization were significantly more likely to die at any time (adjusted hazard ratio=1.15) and especially those with total occlusions and a total of at least two incompletely revascularized vessels (hazard ratio=1.36) [43\*\*].

### **Will these conclusions be altered by drug eluting stents?**

For the two reasons, explained above, it is unlikely that DES or indeed any other type of stent will match the results of CABG for most patients with multivessel or left main CAD. And, indeed, these same reasons are also the most likely explanation of several meta-analyses which report that PCI with stents has no survival advantage over optimal medical therapy in stable CAD [44,45\*\*] and that although, in comparison to BMS, DES reduce the risk of restenosis in low-risk coronary lesions, they do not reduce the risk of mortality or subsequent myocardial infarction [46-49\*\*]. Nevertheless this reduction in restenosis has resulted in DES reaching 90% penetration in some centres and being used in up to 60% of 'off label' indications.

A further consideration is that stent thrombosis appears to be a potentially important limitation of DES associated with an increased risk of myocardial infarction of 65-70% and of mortality of 25% to 45% [50,51\*\*,52]. Although multifactorial in aetiology, the single most important mechanism is impaired endothelialization leaving a potentially prothrombotic substrate within the vessel [53\*\*]. While the precise incidence of stent thrombosis with DES is unknown, the annual risk is estimated at between 1% and 5%, depending on the complexity of the lesion, other patient co-morbidities, and use in 'off label' situations. However the FDA have cautioned that the use of DES is 'associated with increased risks of both early and late stent thrombosis, as well as death and myocardial infarction' [2].

These clinical concerns are compounded by cost implications; not only are DES significantly more expensive than BMS but new recommendations that patients remain on clopidogrel for at least a year [54\*\*] and possibly indefinitely, despite the increased bleeding risks, and at a minimum cost of around a thousand dollars per year will add significantly to costs.

### **Health Economics for Multi Vessel Coronary Disease**

A recent study in the British Medical Journal looked at cost effectiveness of interventions in 1720 patients who were allocated to PCI, CABG or either therapy according to the recommendations of a panel of nine experts and followed for 7 years. It was concluded that while medical therapy and CABG were cost effective at a conventional QALY of £30,000 (\$60,000) PCI was not cost effective and that the additional benefit of stenting over best medical therapy was 'too small to justify the additional cost' [55\*\*]. These findings are consistent with a previous report by the Health Technology Assessment Group in the United Kingdom who also questioned whether the additional costs of DES were justifiable warning that that the



widespread use of DES might 'reduce the gain in quality and possibly the duration of life arising from CABG in the long term' [56].

### **Need for a multi disciplinary teams approach to informed consent.**

The adverse clinical and economic implications of the phenomenal growth in PCI, without an appropriate supportive evidence base, are self evident. Most importantly this strategy has, in effect, denied many patients with multivessel and left main CAD, and particularly diabetic patients, the survival and freedom from reintervention benefits offered by CABG. This reinforces the dangers when a recommendation for stenting is made by an individual interventional cardiologist rather than by a multidisciplinary team (MDT) which should also include a non-interventional cardiologist and surgeon. The MDT should be the minimum mandatory 'standard of care', to ensure that the most balanced and appropriate advice is consistently offered [57,58] and should be enforced by appropriate regulatory bodies and those who pay for coronary interventions.

### **Cautions about future trials of PCI and CABG**

The justification for randomized trials of PCI vs CABG in patients in whom there has been shown to be a strong and consistent survival benefit for CABG (eg left main stem CAD, diabetes, some patterns of multivessel CAD) requires careful consideration because it can be argued that, in the absence of real clinical equipoise between the interventions (ie substantial uncertainty over the risks and benefits of each therapy) such trials may withhold a proven and efficacious treatment [59]. Both Ethics Committees who approve such trials and participating patients must be aware that apparent satisfactory short-term outcomes of PCI are less favourable even within a year and that significant uncertainties about its reliability and durability over the longer term should be weighed against the proven survival benefits of surgery. It is vital, however, that where such trials are conducted that they are powered sufficiently to evaluate mortality as well as other clinically important differences (to avoid an erroneous conclusion that the two interventions are equally effective), that they include at least medium term follow-up of at least five years (as the benefits of surgery accrue with time) and that they maintain a registry of all potentially eligible patients not entered into the trials (to reflect real clinical practice).

### **Conclusions**

Current studies reconfirm that CABG remains the best therapy in terms of superior survival and freedom from reintervention for most patients with proximal left anterior descending, multivessel and left main coronary artery disease (CAD) and that these benefits are magnified in diabetic patients. Furthermore in economic terms PCI is not a cost effective intervention in comparison to medical therapy or CABG. These conclusions are unlikely to be changed by DES which have not been shown to improve survival or freedom from myocardial infarction in any situation and with which uncertainties persist over the precise risk of stent thrombosis. A multidisciplinary team approach to the management of CAD should be enforced as the 'minimum standard of care' to ensure that patients receive the most balanced advice and can make the most informed choices.



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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

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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  $\geq 0.1 \mu\text{g/L}$ . 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 upperlimit 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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## NOTES

# **SO, WHAT IS THE ROLE OF CARDIOPULMONARY BYPASS**

## **IN SURGICAL REVASCULARISATION?**

**Mr. M. Lewis - Royal Sussex County Hospital, Brighton.**

Depending who you address this question to, your answer will range from “none” to “essential”. Off pump CABG usage appears to have levelled out at between 25% to 30% of CABG activity in the US and ≈20% (and possibly falling) in the UK.

Previously, cardiac surgeons have been proud to develop their practice utilising the available evidence base (e.g. adoption of LIMA over saphenous vein as conduit of choice for LAD grafting).

Given these facts, one can, perhaps, make one of several conclusions:

1. Some cardiac surgeons are, for some reason, ignoring current evidence of an overall superior effect of off pump surgery.
2. There is still a perception that the case for off pump is yet to be proven.

My assessment of the large amount of published data on this topic is that it is very confusing! The randomised trials thus far completed have demonstrated broadly comparable outcomes for on and off pump surgery.

Some studies have demonstrated improvements in certain aspects of care with on and off pump surgery. These will be discussed during my talk.

There are very few surgeons who when referred a patient would have no preference as to whether to treat him/her with either off and on pump surgery. This means we all, quite rightly, have an opinion. On occasion, these opinions can become quite firmly held beliefs. This fact alludes to one of the difficulties that has been encountered during the development of off pump surgery; one person’s “early adopter” is another’s Zealot. This taking of positions has, in fact, sometimes discouraged a full debate with the protagonists each retreating to their corners.

Overall the rate of off pump surgery appears to be, at best, static, in the UK. A conclusion might be that what seems to be a formidable learning curve, in an environment of tight scrutiny, has put many people off taking on this new endeavour.

However, large retrospective trials continue to show some benefits of OPCABG over on pump. Is there some sort of bias in these trials or is there really something in off pump surgery?

Perhaps a third possibility (to 1 and 2 above) is that there are cases for which off pump is more suitable and those for which on pump is better. Surgeons clearly need more data to be able to take an informed decision and offer the appropriate treatment to patients on an individualised basis.

Providing the clear evidence base for this decision making process is the challenge that lies ahead.



## **THE EVIDENCE BASE FOR CONDUIT CHOICE**

Clinical outcomes after coronary artery bypass (CABG) are in part dependant on continuing graft patency. Graft patency is affected not only by the nature of the conduit but also by the artery to which it is grafted. Great care has to be taken in interpreting studies that selectively catheterise patients after CABG and use this data to calculate patency rates; there is enormous potential for selection bias. Studies reporting clinical outcomes may be more reliable but if not randomised are subject to selection bias in allocating patients to receive different conduits.

Despite these reservations the following observations are reasonably robust. The advantage of placing the left internal mammary artery (LIMA) to the left anterior descending artery (LAD) is established. Although patency of saphenous vein grafts, and by inference clinical outcomes, may be improved in contemporary series, the available evidence supports more extensive use of arterial conduits.

Placing both right internal mammary artery (RIMA) and LIMA to the left sided coronary arteries reduces the hazard ratio for death to 0.81 compared to a LIMA alone (1). This benefit is evident up to 20 years and persists regardless of age and left ventricular function (2).

Patency of the radial artery is best when it is placed to left sided vessels with at least 70% stenosis. Under these conditions patency approaches that of IMA grafts (3). In general the patency lies between saphenous vein grafts and internal mammary arteries (4). Midterm clinical outcomes may be improved if it is used as a second arterial graft rather than saphenous vein (5) and may be equivalent to use of the RIMA (6). The gastroepiploic artery should not be used (7) routinely.

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# SURGICAL MANAGEMENT OF HEART FAILURE

## STRUCTURE/FUNCTION RELATIONSHIPS BETWEEN FIBER ORIENTATION AND VENTRICULAR EFFICIENCY

### **Structural Considerations**

The conical pattern of normal heart size and shape is well known since Hippocrates and Galen, and was described by the forefathers of anatomy. More importantly, a helical spiral at the cardiac apex was demonstrated by Lower in the 1600's, an internal helix was postulated by Senec in the 1700's, and described as the Treibwerk by Krehl in the 1891 (1). Until recently, this helical intrinsic form was not proven, and inability to unfold the heart's basic structure was considered to reflect the "Gordian Knot" by cardiac anatomists. Studies by Francisco Torrent-Guasp began in 1950 (2) and have finally unraveled the cardiac structural pattern. Torrent-Guasp spatially unfolded the intact heart to demonstrate a rope like model, that contains a myocardial fold that separates heart structure into two simple loops named the basal and apical loops. The muscular myocardial band begins at the pulmonary artery and ends at the aorta. The structural components include a horizontal or transverse fiber orientation for the *basal loop* that surrounds the right and left ventricles, and a change in fiber direction through a spiral fold in the ventricular band to cause a ventricular helix that now contains obliquely oriented fibers that form a descending and ascending segment of the *apical loop* with an apical vortex. These components and the implications of this model were discussed in a recent NIH workshop (3).

Surgical correction of the dilated heart requires changing the spherical configuration architecture into a more normal elliptical form (4;5). The architectural patterns of the normal and dilated hearts define a) the *transversely* oriented fiber arrangement of the basal loop that surrounds the normal helix that is comprised of an apical loop with *obliquely* oriented fibers reciprocally arranged in an approximate 60 degree angle and b) the spherical geometry of a failing heart, whereby the basal loop is intact but stretched, and continues to surround a more spherical fiber arrangement of apical loop fibers that develop a more transverse fiber arrangement, so that the fiber orientation of the apical loop becomes less oblique to now more closely resemble the horizontal basal loop. Examples of this rearrangement of apical loop fibers to a more transverse, or circumferential pattern will be shown from the corrosion cast studies of Gorodkov in Moscow. A form related background for rebuilding ventricles that stems from the spatial orientation of cardiac fibers that suggest the failing ventricle becomes functionally impaired when the normal obliquely orientated helical heart fibers become more horizontal when muscle stretches into the spherical form. (6;7)



## Structure /Function

The bioengineering infrastructure for this mechanical change in size and shape is rebuilding more oblique fiber orientation. This anisotropic configuration requires a conical form, whereby the increased deformation responsible for contractile strain improves from the widened base to the helical apex vortex ((8)). The pattern of ejection and filling are related to a sequential twisting of the LV to eject and rapid untwisting to suction venous return to rapidly fill (9). These normal twisting patterns were originally described by Borelli in 1660 (10), and are visible at operation or by MRI recordings.

Basic scientific studies set the precedent for this geometric component, by establishing how the normal 15% fiber shortening of isolated muscle strands is changed when an integrated fiber orientation exists within the intact heart (11;12). Ejection fraction is 30% if fiber orientation is transverse, and increases to 60% with oblique fiber direction, as deformation increases during transition from midwall to apex. (11). This functional pattern is evident on DENSE MRI studies that displays the transverse and oblique fiber orientation of the basal and apical loops. More importantly, the stretched dilated heart loses the normal twisting pattern, and a constriction and dilation pattern define functions to correspond to the stages that were deduced by William Harvey from pivotal anatomic but not functional dissections that showed the pulmonary circulation (15).

These global considerations apply for normal fibers, whereas damaged stretched hearts contain sites of fibrosis or excess collagen formation that can limit the expected improvement after changing ventricular form. A clear contrast between ischemic and non ischemic dilated failing ventricles is provided by precise infarct location that identifies the abnormal regional site after coronary occlusion. In this ischemic cohort, the remote, non infarcted muscle stretches to allow compensatory function. Conversely, a more global process exists in non ischemic patients, whose architecture has variable site location (16-18). This inhomogeneity in a global process must direct efforts at uncovering the predominant region responsible for chamber stretching, and simultaneously uncovering how remote regions with less intrinsic disease compensate to support cardiac output. Localizing major segments of intrinsic disease is essential, since efforts at rebuilding must concurrently provide a) an elliptical shape to the abnormal spherical structure, and b) exclude predominant regions of damaged muscle fibers responsible for causing this global widening.

From a sports perspective the normal heart is like a football, where a spiral motion is generated from passing the elliptical shaped contour. Conversely, the basketball, with a spherical configuration defines the shape of the dilated heart, whose efficiency is diminished by abnormal form, and this ineffective action is independent from the person passing the ball ; structure, not player is at fault .

A biologic example of the sports paradigm defines the elliptical pattern of the normal heart with a football like shape, the spherical architecture of an ischemic heart were a basketball like shape results from infarction of the apico-septal regions, and this form leads to restoration to surgically rebuild the elliptical form to return architecture back towards the normal football like configuration.



## Implications with Helical Fiber Orientation

The helical architecture of the normal heart has been confirmed by strain relationships using MRI (19), corrosion casts showing spiral architecture,(20) and by sonomicrometry crystals (21); each pattern reflects the normal oblique fiber orientation that conveys maximum force during ejection and suction. These observations coincide with the helical heart configuration, and change when dilation alters this architecture because of flattening of the double helical arms of the apical loop.

Prior sonomicrometer crystal recordings document the importance of obliquity to achieve the maximum extent of directional shortening (21). This functional framework nicely coincides with conceptual determinants of efficiency of ejection fraction (EF), 60% EF is expected with oblique fiber direction, a value that falls 30% EF with transverse or horizontal fiber direction (11). Although fiber orientation is oblique, recordings from crystal tracings seem to reflect spiral coils within the fibers (*or coils within coils*) to obtain maximal efficiency (22). Conversely, reduced shortening develops with a more horizontal position for crystals placement (21).

These shortening patterns closely link with changes in ventricular shape following reconstruction methods that address “disease versus form”. The patch position is flatter in ischemic disease when the scar becomes the only marker during ventricular shape rebuilding and may result in a more spherical chamber. Conversely, a more conical chamber is created when “form” becomes the guideline for patch placement; obliquity now becomes the marker for patch insertion and conceptual goal of the insertion policy. Future comparisons of ventricular function by MRI tagging are needed to define the extent of deformation, and evaluate the validity of this form reconstruction objective.

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# PATHOPHYSIOLOGIC IMPLICATIONS OF THE VENTRICULAR

## MYOCARDIAL BAND (Helical Heart)

The conical pattern of normal heart size and shape is well known since Hippocrates and Galen. More importantly, a helical spiral at the cardiac apex was demonstrated by Lower in the 1600's, an internal helix was postulated by Senec in the 1700's, and described as the Treibwerk by Khrell in the 1800's(1). Until recently, this helical intrinsic form was not proven, and inability to unfold the heart's basic structure was considered to reflect the "Gordian Knot" by cardiac anatomists. Torrent-Guasp spatially unfolded the intact heart to demonstrate the presence of a myocardial fold that separates heart structure into two simple loops named the basal and apical loops that start at the pulmonary artery and end at the aorta.(2) The structural components include a horizontal or transverse fiber orientation for the *basal loop* that surrounds the right and left ventricles, and a change in fiber direction through a spiral fold in the ventricular band to cause a ventricular helix that now contains obliquely oriented fibers that form a descending and ascending segment of the *apical loop* with an apical vortex.

### **Structure / Function**

Understanding of myocardial function must incorporate knowledge of underlying structure to allow a clear structure / function relationship to emerge, with a key ingredient that relates into how fiber orientation of the septum impacts right and left ventricular performance. The presentation will to 1) define the components of septal architecture and demonstrate that they are explained by the model of the helical ventricular myocardial band (3) 2) demonstrate the structure function relationship that results from preservation of the normal anatomic framework, 3) describe how distortion of this anatomic framework by lesions of the left or right side of the heart can impair biventricular function, 4) define how stretch of the septum with bowing of its thick structure into either left or right ventricle can create an "architectural disadvantage" that impairs septal contractile function, 5) indicate how restoration of normal anatomy will return septal function toward normal and thus improve biventricular performance, providing excitation contraction coupling is not impaired, 6) identify the importance of a sequential activation of the septum and it's effect on cardiac dynamics, especially in regard to resynchronization, and 7) demonstrate why the septum is the "motor of biventricular function", and "the lion of right ventricular function.

Sallin (4) and Ingels (5) furnished physiological studies that confirmed the importance of fiber orientation, by relating the effects of different angulations to expected ejection fraction. Basic science studies of myocyte function done on isolated fibers from muscle strips in a Petrie dish show that the maximal shortening of these fibers is 15%. The intact heart, however, has a continuum of muscle wrapped in a pattern that alters fiber orientation in different myocardial regions. Ejection fraction is 30% if the fibers are transverse, as occurs in the free wall of the right ventricle and increases to 60% if there is predominant oblique fiber orientation, a pattern that comprises the septum and free wall of the left ventricle beneath the



external wrapping of the left segment of the basal loop . The characteristic motion of twisting of the septum is linked to the anisotropic form created by this oblique fiber orientation . *Fiber orientation therefore accounts for both aspects of RV function that includes a) bellows like action resulting in compression, caused by the transverse basal loop and b) twisting due to oblique sequential septal contraction.*

The twisting action disappears when the cardiac chamber dilates and the septum gets bowed into the right ventricle by left sided lesions such as aortic or mitral insufficiency, dilation from ischemic or non ischemic congestive heart failure, or rhythm interruption from wide QRS or left bundle branch block. Similarly, right sided lesions like pulmonary insufficiency, atrial septal defect, or pulmonary outflow tract obstruction bow the septum toward the left side. The central theme (6;7) is that each event disrupts normal architecture by stretching the septum so that a more transverse, rather than oblique fiber orientation comprises it's spatial configuration and subsequently disrupts it's sequential twisting function needed for maintaining cardiac output into an increased resistance vascular bed. Of great importance to the cardiac surgeon is the introduction of septal dysfunction due to "septal stunning " that arises from impaired protection strategies during correction of underlying mechanical defects.

### **Clinical Examples**

Two examples in the category of congenital heart disease include a) early or late development of right heart failure following a procedure that reduced pulmonary hypertension by correcting a defect, and b) septal dysfunction by stretching from a volume overload, as with pulmonary insufficiency.

In the first instance, the septum had normal function preoperatively , despite pulmonary hypertension. Loss of the septal twist from stunning will either 1) limit right heart performance intra operatively if pulmonary hypertension persists, or 2) evolve postoperatively if pulmonary pressure is lowered, as the RV constrictive property of the basal loop is preserved to maintain efficient cardiac output. . However, RV failure supervenes in the ICU if delayed pulmonary vasoconstriction, because twisting capacity is impaired by septal stunning. The solution is to study septal motion intra operatively, and determine if the method of protection allows normal post operative function. If it does not, an alternate protective method should be sought.

In the second instance, septal stretch by RV volume overload will alter fiber orientation by bowing, and impair septal twist. This is frequent finding in patients with pulmonary insufficiency and right heart failure after repair of Tetralogy of Fallot, and clear from preoperative absence of septal shortening or late thickening by echo study. The solution to this "architectural septal stretch disadvantage" is supplementation of procedures that are used to restore valvular competence , with new approaches that



include restoration of the septum into a mid line position , while avoiding it's injury by safe protective techniques. . A “ ventricle-valve” approach is needed, and an example will be shown(8).

### **Implications**

Understanding of the central role of the septum in RV function provides the theoretical basis for treatment of entities such as right ventricular infarction and post cardiac surgery RV dysfunction. Knowledge of the anatomy and physiology of the septum also allows the rational design of operations to treat various cardiac conditions such as RV dysplasia, RV failure from pulmonary insufficiency, transplantation RV dysfunction, right sided congenital defects that affect LV function, techniques of myocardial protection, planning physiologic treatment of RV dysfunction by use of a structure / function relationship, and for left ventricular restoration. The septum is the “lion of RV function” and further understanding of its role as a component of the helical ventricular myocardial band will alter thinking about surgical management.

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# THE ROLE OF RESTORATION, REVASCULARISATION AND REPAIR

## “SURGERY FOR HEART FAILURE” OR

## “CAN YOU MAKE A SILK PURSE OF A SOW’S EAR?”

Heart failure is common, an increasing burden on health care, and with an ageing population, will become a greater problem. The number of patients in the USA at the severe end of the spectrum (estimated at 200000) is 100 times greater than the annual number of heart transplants (approx 2000). This ratio will be even worse in the UK, where we perform only a quarter as many transplants. In both countries, this procedure is already restricted to the sickest patients, usually in hospital and on inotropes. Mechanical devices do not yet have the requisite durability and biocompatibility to be more than temporary solutions.

The effectiveness of “medical therapy” with a range of proven drugs, but also including resynchronisation and implantable defibrillators, continues to improve, certainly with regard to survival. But there is clearly room for additional measures, and surgical options are repeatedly proposed for some of these patients.

There is no doubt that for modest degrees of cardiac dysfunction, correction of obvious lesions – critical coronary stenosis or significant mitral regurgitation - is of benefit both in terms of relieving symptoms and improving life expectancy. Correction of severe MR with valve repair, even in asymptomatic patients, restores normal life expectancy; uncorrected patients have more heart failure and a poorer prognosis. There are many who claim that this improvement, particularly in LV shape and size – described as “remodelling” – can be extended to more severely affected patients. The rationale is sound – reduce preload, allow the ventricle to be smaller, and the survival will be better. But does it work for the most severely affected? Is it a substitute for transplant, and can it delay or avoid the future need?

These are two separate questions, but answers to both are lacking. Dion’s group have shown that reduction mitral annuloplasty is effective for both ischaemic and non-ischaemic cardiomyopathy with significant MR, but only up to a certain size of ventricle. The worst patients neither re-modelled their ventricles or had a survival benefit. We do not know whether the better patients had a survival benefit, but some, admittedly retrospective data from the US suggests they did not. For those with the biggest ventricles, one option is to add a restraining device. In his description of the Acorn trial, Acker states that “...CSD (cardiac support device) reverses the natural history of heart failure..and represents a new and effective approach for patients with enlarged hearts” But the improvements were modest. Of those with concomitant mitral repair, only 5% were in NYHA. This trial showed that these patients can be operated on with very low risk (1.3% mortality) but gives us very little data on the sickest patients.

The same arguments extend to “LV restoration” the collective term for operations which re-shape the ventricle, of which the Dor procedure is now the best known. This is principally applied to the sequelae of large anterior infarcts, and improvements in LV size and NYHA grade are claimed. But the studies are single centre, with an undeniable selection bias, and retrospective. A recent Brazilian paper suggests that restoration with CABG for viable myocardium is better than either procedure if isolated. But entry criteria were restricted only to EF<50%!

Thus at the earlier stages of heart failure, surgical results are good, with low mortality, and *some* evidence of geometric advantage. For many patients there may be symptomatic advantages. But the suggestion that prognosis is improved and later failure prevented is entirely unproven, and will remain so until prospective trials against the *best* of medical therapy can be performed.

For the most severely affected, the evidence is either lacking, or suggests little advantage to a high-risk procedure. The history of the Battista operation is a lesson for all in this field.

If the myocardial reserve is too depleted to achieve a good result, can we add to it. Autologous stem cells,



principally injected at the time of myocardial infarction, but also used in conjunction with conventional surgery, clearly have some effects. But the benefits have been very limited, and no one approach has a proven role.

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# ASSESSMENT FOR CARDIAC TRANSPLANTATION

**Professor J. Dark – Freeman Hospital, Newcastle upon Tyne.**

The numbers with advanced heart failure are huge, and only a very small proportion will be accepted for transplant. The key to assessment is to identify those with end-stage disease that really is refractory to the whole range of medical and even surgical treatments, but still with the potential to survive the procedure and return to a good level of function.

Diagnoses are divided between various cardiomyopathies (45%) and ischaemic disease (also 45%), with a smaller number with congenital or valvular disease. Most of those with cardiomyopathy will have the dilated, idiopathic variety. There will be smaller numbers with restrictive and occasionally hypertrophic physiologies. In units with a paediatric and adolescence referral there will also be patients with the heart failure related to muscular dystrophy and post anthracycline chemotherapy induced damage. In a paediatric practice, patients are equally divided between structural congenital heart disease and cardiomyopathy.

Some patients with ischaemic disease will be transplant candidates as a consequence of intractable arrhythmias. In an era of increasing availability of mechanical devices, we come across some young post infarct candidates, rescued from cardiogenic shock, and with transplant as the only reasonable next step. But barely 100 adult transplants are now performed annually in the UK, and we are already approaching the situation where a significant proportion of the transplants done are in VAD patients, with a range of additional risks and technical difficulties.

Before transplant is considered, it is important to have explored all the medical options. These include the full range of drug treatments, including B blockers and spironolactone in addition to ACE inhibitors and loop diuretics. Surgically remediable conditions such as occult aortic stenosis must be excluded, and the possibilities for high risk revascularisation or ventricular restoration must be fully explored. In addition many patients can be improved with re-synchronisation.

Investigations include all the standard workup of a patient for complex surgery. In addition, patients should undergo measurement of maximal oxygen uptake on exercise (VO<sub>2</sub> max). It is easy to underestimate functional capacity, so patients must reach their anaerobic threshold at 50-60% on VO<sub>2</sub> max. A value of less than 14ml/Kg /min has been traditionally associated with a poor prognosis. This value, and the resulting concept of a “heart failure score” was derived by studies in the era before routine B blockade and AICD implantation. In the current era, stable patients with such a value can be safely observed. For stable patients there is no survival advantage to transplant, as was clearly demonstrated in a German study a few years ago.

All potential candidates should undergo right heart cath and calculation of pulmonary vascular resistance (PVR) and transpulmonary gradient (TPG). A PVR of more than 4 Wood units, or a TPG of more than 12-15 are regarded as contraindications because of the risks of acute right heart failure post transplant. There is however increasing realisation that PVR may vary from week to week and much of the right heart problem is donor related. There is no doubt that patients with high, fixed pulmonary pressures represent a high risk group.

Finally, a measure of pre-transplant anti-HLA antibodies is required. Recipients who have been exposed to blood transfusion, pregnancy, previous surgery with homografts or VADs may have varying titres of such antibodies. Precise specificities can be defined by current bead based (Luminex) techniques, identifying the HAL epitopes to be avoided in the donor. Recipients with a very high reaction frequency, defining the proportion of potential donors to be avoided, may be very difficult to transplant.



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## VENTRICULAR ASSIST DEVICES

Ventricular Assist Devices (VADS) offer mechanical support to the failing left (or right/or both) ventricle to restore 'cardiac' output and organ perfusion. There are now many devices available (current third generation) and they can be classified into implantable/extracorporeal and pulsatile/continuous flow. In the UK three centres are designated to provide VAD therapy. In most cases VAD support is used as a 'bridge' to transplantation in situations when a heart is not immediately available, or when raised PVR or other temporary end organ dysfunction precludes heart transplantation. There is some evidence for recovery of cardiac function in a minority of patients supported with VADS. As VADS become more reliable and donor organ availability continues to decline the prospect of VAD support as permanent chronic therapy becomes real, although at present there is not enough evidence to justify the resources necessary. The outcome depends on the patient population supported and complications include bleeding, infection, embolism and device failure. Short term simple devices can be used in post cardiectomy patients and occasionally those in multiorgan failure.

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# ANATOMY OF THE MITRAL VALVE

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

## **General Anatomy**

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.

## **Mitral annulus**

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.

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.

## NOTES

# MITRAL VALVE DISEASE: AETIOLOGY OF DISEASE AND DEFINITIONS

## 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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# **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 a homogeneous cohort of 208 patients <sup>ii</sup>, other surgical techniques have been required: a sliding plasty in 98 patients, use of artificial chordae in 5 patients, papillary muscle shortening in 4 patients and removal of posterior annulus calcifications in 5 patients. These techniques resulted in a 100% rate of repair for this lesion for an operative mortality of 2.9% and a 6-year survival of 87%.

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>iii</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>iv</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. The trend nowadays<sup>v</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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# **MITRAL REGURGITATION: THE EVIDENCE FOR INTERVENTION**

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

It is quite clear that symptomatic severe mitral regurgitation carries a poor prognosis if left untreated. Successful mitral valve repair can both eliminate symptoms and improve prognosis. Mitral repair, where possible, is superior to mitral valve replacement in terms of both operative mortality and long term outcome. All these issues are dealt with comprehensively in the ACC/AHA guidelines<sup>1</sup>.

Decision- making in asymptomatic mitral regurgitation is less clear. Over the last couple of years there have been 2 important publications. Enriquez-Sarano et al<sup>2</sup> analysed a large series of patients with asymptomatic mitral regurgitation and found that the severity of MR as measured by effective regurgitant orifice area was an important predictor of outcome. They suggest that patients with an EROA > 40mm<sup>2</sup> should undergo surgery irrespective of symptoms, LV size or function. Rosenhek et al<sup>3</sup> looked at a group of asymptomatic patients with severe MR and followed them by 'watchful waiting' and operated only at the onset of symptoms, atrial fibrillation, pulmonary hypertension, LV enlargement (LVESD > 4.5) or LV dysfunction. The whole group had an outcome as expected and less than 1/3 of patient needed surgery over the period of follow up.

The updated ACC/AHA guidelines<sup>1</sup> give an LV size threshold for recommending intervention has decreased from 4.5 to 4.0 cm and they suggest that surgery is reasonable for asymptomatic patients with normal LV size and function in experienced centres in which the likelihood of successful repair with residual regurgitation is greater than 90%.

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3. Rosenhek R et al Outcome of watchful waiting in asymptomatic severe mitral regurgitation. Circulation. 2006 May 9;113(18):2238-44. Epub 2006 May 1.



# **MITRAL REGURGITATION: THE EVIDENCE FOR INTERVENTION**

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

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# **TRICUSPID VALVE: THE EVIDENCE FOR INTERVENTION AND OPERATIVE TECHNIQUES**

**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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## SECONDARY MITRAL REGURGITATION: ROLE OF ECHOCARDIOGRAPHY

Secondary mitral regurgitation (MR) is, by definition, a mitral valve dysfunction with apparently “normal” mitral valve, caused by a ventricular disease: ischemic (“ischemic” IMR) or non ischemic disease as dilated idiopathic cardiomyopathy or aortic valve disease cardiomyopathy (“functional” FMR). It is opposed to organic MR where the LV dysfunction is a consequence of a primary mitral valve disease.

*Ischemic/functional MR is a ventricular disease and not a valvular one.* It explains why this frequent disease (10 to 20%) is also a life threatening disease associated with a significant excess of mortality, it represents furthermore an independent predictive factor of mortality (vicious circle). The evaluation of these MR has to be complete: rest echocardiography plays a major and pivotal role: it permits the diagnosis (MR often silent) and their quantification: severe MR in ischemic/functional context has specific cut-off values (in comparison with organic MR) : ERO  $> 20$  mm<sup>2</sup> (vs 40 mm<sup>2</sup>), Regurgitant volume  $> 30$  ml (vs 60 ml) and Vena Contracta Width  $> 4$  mm (vs 7 mm), criteria classically considered as “moderate” MR. For the quantification of ischemic MR exercise echocardiography is critical and may increase the severity of there intermittent MR: it represents a diagnostic but also a prognostic value (when ERO difference is superior to 13 mm<sup>2</sup>). The Echo Dobutamine is more dedicated to assess myocardial viability and contractile reserve in ischemic/functional MR. MRI and/or MRI Dobutamine is also a critical tool to determine myocardial viability and almost precise the LV geometry (local or global deformation) and papillary muscle (PM) displacement. (post and/or ant). Despite the complexity and diversity of underlying mechanisms, Echo and/or MRI permits to classify ischemic MR in 2 main groups: asymmetric (A) where the jet is eccentric, origin localised on P3 scallop with a local LV deformation (inferior) and PPM displacement with a moderate LV dysfunction and a symmetric one (S) where the jet is central with a global deformation of an enlarged LV and both PM displacement with a seagull sign of the anterior leaflet (A2), with a severe LV dysfunction (EF  $< 35\%$ ). This last group of IMR (symetric) is very similar to functional MR by echocardiography. The tricuspid and RV assessment has not to be forgotten (annular dilatation ++). BNP may be also very useful in this group of patients to evaluate more objectively their functional status. Treatment of Isch/Funct MR is logical because it interrupts the vicious circle induced by MR on LV dilatation and dysfunction. The impact on mortality is still controversial. Because IMF/FMR is ventricular disease, the treatment has to be integrated in the scope of heart failure therapy. It is now very well demonstrated that beta blockers and/or resynchronization therapy may improve some FMR. Percutaneous approaches are being developed and might be useful in some group of patients, but it is still controversial and in evaluation. The surgical treatment is the most appropriate treatment to correct completely these MR but it requires a very precise and complete evaluation by the cardiologist: symmetric or asymmetric group, precise location of the jet (P3 or all post scallops), LV dimensions (particularly if ESD is above 55 mm), EF, results of stress testing, precise LV and subvalvular geometry by MRI, myocardial viability and contractile reserve, tricuspid annulus dilatation ( $> 40$  mm).... In these conditions surgeons are able to provide the best surgical approach for an individual patient: in the asymmetric group of IMR undersized (2 sizes) or ischemic ring annuloplasty is logical. In symmetric IMR and Functional MR undersized annuloplasty (2 sizes) or specific ring is also logical. The most important criteria to obtain in all groups of secondary MR is a coaptation distance  $> 8$  mm measured intra-operatively by TEE. In some cases when LV enlargement is critical, LV procedures may be associated (CorCap, PM sling, Ventriculoplasty....), when there is a seagull sign of anterior leaflet (A2) chordal cutting has been proposed. Cellular cardiomyoplasty was also recently proposed.

Secondary MR is a severe disease which has to be precisely evaluated by cardiologists in order to provide critical informations for the best surgical approach. Percutaneous options and impact on survival are still controversial and need further prospective evaluation.



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

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 ml, but in ischaemic MR a regurgitant volume of greater than 30 ml 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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# **ISCHEMIC MITRAL VALVE REGURGITATION:**

## **THE LIMITS OF OUR KNOWLEDGE**

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The field of ischemic mitral regurgitation continues to evolve with recent studies improving our understanding of the pathophysiology and outcomes. Current approach to therapy should consist of definitive diagnosis by clinical and echocardiographic criteria, complete surgical revascularization, and restrictive annuloplasty using complete rigid or semi-rigid rings. Consistent application of surgical technique and collection of robust outcomes data is crucial to guiding our understanding of the natural history of surgically treated disease. Unfortunately limitations in surgical techniques and flaws in study methodology have restricted the ability of the literature to determine the efficacy of mitral valve annuloplasty and although many papers suggest annuloplasty is of limited efficacy, these papers have critical flaws. The efficacy of alternative surgical techniques such as chordal cutting, valve replacement and papillary muscle relocation is undetermined. This lecture will review recent developments and controversies regarding the pathophysiology and management of ischemic mitral regurgitation and also discuss the limitations of the published literature.

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**SURGICAL ATRIAL FIBRILLATION ABLATION:**

**Indications, Operative / Postoperative Strategy & Results**

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## 1. Executive Summary

Atrial fibrillation (AF) is a cardiac arrhythmia (abnormal heart rhythm) with a recently reported prevalence of 1.15% in the general population. Furthermore, prevalence is increasing and people with AF are 5-7 times more likely to have a stroke, twice as likely to die and make significant use of healthcare resources compared to people with no AF. It is important for healthcare commissioners to find more effective ways of managing AF in order to contribute to meeting mortality and health gain targets and to control escalating costs.

There are inherent problems with conservative treatment options for AF. Firstly, studies have shown that antiarrhythmic drugs do not deliver much better rates of sinus rhythm than controls. Secondly, the drugs are associated with a high level of toxicity and serious complications, so tolerance and uptake are poor. Thirdly, the efficacy of drugs reduces over time. Finally, drug management becomes an expensive option for many patients when the duration of treatment; the cost of monitoring and treating adverse effects of drugs; the costs of repeated cardioversions, A&E visits and emergency admissions are taken into account. To deliver NICE guidance, commissioners face spending significantly more on drugs to treat AF and anti-coagulants.

NICE guideline 36 (Atrial Fibrillation) recommends that referral should be made for further specialist intervention (i.e. interventional procedures/surgery) in patients for whom pharmacological therapy has failed. It also recommends that AF surgery should be considered for patients undergoing mitral valve repair (concomitant AF surgery) and when pharmacological therapy and interventional procedures have failed (lone AF surgery).

An appraisal of the available evidence supporting surgical and cardiology procedure options reveals that radiofrequency ablation (modified Maze procedure) for AF, carried out in conjunction with mitral valve repair, promises to be superior in meeting all five of the primary goals of treatment for AF: Reversing the risk factors that cause atrial fibrillation; slowing the heart rate; preventing strokes; converting AF to normal heart rhythm and preventing recurrence. In addition, the response to treatment appears to be durable over time, with low rates of reoccurrence and an observed decrease in dependence on pharmacological therapies. See Appendix 2: Option Appraisal in conjunction with Appendix 1, which sets out the indications for alternate surgical and interventional cardiology options.

Without direct economic evidence comparing alternative treatments, a predictive financial model has been developed using assumptions based on published data. The model (attached) demonstrates that although concomitant surgery for AF will increase the cost of mitral valve repair above tariff, the investment should be more than off set by predicted savings against drug costs, admissions, defibrillation and the incidence of repeat procedures. The relative cost of care for patients undergoing concomitant RF ablation in both year one and the first five years after surgery compares well in relation to other invasive treatments.

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## **2. Background**

### **2.1 PREVALENCE AND INCIDENCE**

Cardiac arrhythmia affects more than 700,000 people in England and is consistently in the top ten reasons for hospital admission, using up significant A&E time and bed days. Atrial fibrillation (AF) is the most common type of abnormal heart rhythm. Prevalence of AF is around 1.15% overall (Majeed et al, 2001) and between 4.7% (NICE guidelines – Newcastle Survey) and 5.9% in those over 65 (Feinberg, 1995). Prevalence is increasing across all ages and by 2050 it is expected that the increase will be 2.5 fold (Waldo, 2003).

### **2.2 PATHOPHYSIOLOGY, SYMPTOMS AND PROGNOSIS**

In people with AF, electrical impulses don't follow a normal pathway through the heart. As a result, the heart doesn't beat properly or pump blood correctly. Although it is often associated with heart disease it can occur in patients with no detectable disease. Many people with AF live for years without problems, whilst others suffer palpitation, dizziness, chest pain, breathlessness, poor effort tolerance and lack of energy. Over time haemodynamic impairment and thrombotic events result in significant morbidity, mortality and cost.

### **2.3 IMPACT ON RISK OF STROKE AND PROGNOSIS**

**WITH AF, STROKE IS 5-7 TIMES MORE LIKELY**

It is thought that increased risk of stroke is caused by hypertension, which reduces the speed of blood flow in the left atrial appendage and predisposes to clot formation (Fuster et al, 2001). Over 90% of these embolic strokes are from clots originating in the left atrial appendage (Johnson et al, 2000).

If the clot is pumped out of the heart, it can travel to the brain, resulting in a stroke. Clots can also travel to other parts of the body (kidneys, heart, intestines), causing damage.

- The rate of ischemic stroke for patients with AF is around 5% per annum (Fuster et al, 2001).
- AF is responsible for around 15% of all strokes (Falk et al, 2001 and Ezekowitz et al, 2003) and 45% of embolic strokes (Gersh et al, 2005).
- In people over age 75, AF is the most important single cause of ischemic stroke. (Hart and Halperin, 2001)
- AF doubles the probability of a stroke resulting in permanent disability or handicap (Lamassa et al, 2001).

In 2004/5, there were just over 122,000 admissions for strokes in England, not attributed to haemorrhage, with an average length of stay of 27.9 days. Application of Gersh's rate to this data (2005) means that just under 55,000 admissions for stroke may have been attributable to AF, accounting for just over 4,600 beds occupied throughout the year across England. This is equivalent to 8 medium sized district general hospitals.

Kimura (2005) found that patients admitted with stroke who had AF had a median NIHSS (National Institute of Health Stroke Scale) score of 12 compared to a score of 5 for patients without AF. It is therefore likely that the average length of hospital stay for someone admitted for a stroke with AF would exceed the average. Mortality within 28 days of admission was 11.3% for the AF group and 3.4% for the non AF group.

## **2.4 IMPACT ON HEART FAILURE**

**AF CAN CAUSE HEART FAILURE**

AF can decrease the heart's pumping ability by as much as 20 to 25 percent (Cleveland Clinic Heart Centre, 2006). AF, combined with a fast heart rate over a long period of time, can result in heart failure.

## **2.5 IMPACT ON MORTALITY**

**RISK OF DEATH IS ALMOST DOUBLED**

AF is an independent risk factor for death with a relative risk of 1.5 in men and 1.9 in women, after adjustment for associated cardiovascular disorders (NICE, 2006). The drugs used to treat AF, i.e. Digoxin and anti-arrhythmic drugs, are also associated with a 30-50% increase in mortality (Corley et al, 2004).

## **2.6 IMPACT ON HEALTHCARE COSTS**

**DEMANDS ON HEALTHCARE RESOURCES ARE SIGNIFICANT**

Stewart et al (2006) reported that the rate of incident hospitalisation for AF in the Renfrew/Paisley population database was 1.9 cases/1000 person years. In one series, AF accounted for 34.5% of patients admitted with a cardiac rhythm disturbance (Bialy et al, 1992). Wattigney et al (2003) noted a 2-3 fold increase in hospitalisations for AF in the US between 1985 and 1999. In 1999, the proportion of patients discharged to long term care rather than home were 15% for men and 23% for women.

## **2.7 IMPLICATIONS FOR SERVICE PLANNING AND COMMISSIONING**

These factors create an imperative to manage AF more quickly, more cost effectively and in appropriate settings. In recent years there have been significant improvements in both technology and clinical skills that are enabling improved prevention, diagnosis and treatment of AF. Implantable cardioverter defibrillators (ICDs) and sophisticated pacing devices have given cardiologists many more treatment options for these patients. In addition, catheter ablation, which treats malfunctioning parts of the heart, can provide a cure so that patients no longer require medication or suffer from palpitations.

### 3. Strategic Context

#### 3.1 NATIONAL GUIDELINES

The management of atrial fibrillation is covered by “NICE Guideline 36: Atrial Fibrillation” published in 2006 and the National Service Framework for Coronary Heart Disease Chapter 8 on cardiac arrhythmias, added in 2005. The Healthcare Commission assesses the performance of NHS organisations in meeting core and developmental standards set by the Department of Health in “Standards for Better Health” issued in July 2004. The implementation of clinical guidelines forms part of the developmental standard D2. Core standard C5 says that nationally agreed guidance, such as NICE guidance and NSFs, should be taken into account when NHS organisations are planning and delivering care.

NICE states that the ultimate responsibility for implementing this guideline rests with the chief executives and that clinical governance mechanisms should ensure that action plans and progress with the implementation of this guideline are reported back at individual board level. They advise that areas of non-compliance should be recorded.

NHS Organisations are advised to take the following implementation steps:

1. Appoint an implementation lead & establish an implementation group through the local cardiac network
2. Disseminate the guideline
3. Carry out a baseline assessment
4. Assess costs and savings
5. Establish an action plan

Although a comparison of interventional procedures is outside the scope of the guideline, the guideline includes the following recommendation:

#### **NICE RECOMMENDATION**

Referral for further specialist intervention (i.e. interventional procedures/surgery) should be considered in the following patients:

- those in whom pharmacological therapy has failed **B**
- those with lone AF i.e. no structural or ischaemic heart disease **B**
- those with ECG evidence of an underlying electrophysiological disorder (eg Wolff Parkinson–White syndrome). **C**

In addition, NICE makes the following comments about the criteria for success for alternate procedures:

#### **Pulmonary vein isolation (PVI)**

Patients with the following characteristics may benefit from referral for PVI: Patients resistant to pharmacological treatment; younger rather than older patients or those with lone AF. Percutaneous radiofrequency ablation, the standard approach, is covered by **NICE IP Guideline 68 (2006)**.

#### **Pacemaker therapy**

Other than recognised indications for pacemaker implantations such as sinus node disease, symptomatic bradycardia and chronotropic incompetence, no evidence was found to specifically identify other patients with AF who should be referred for pacemaker implantation.

## **Arrhythmia surgery**

The NICE clinical guideline recommends surgical treatment of AF for patients undergoing concomitant cardiac surgery (eg mitral valve surgery). In addition, NICE Interventional Procedure (IP) Guidance has been published on various forms of ablation for AF during other cardiac surgery:

### **IPG 21: Radiofrequency ablation (NICE, 2005)**

### **IPG 22: Microwave ablation (NICE, 2005)**

### **IPG 23: Cryoablation (NICE, 2005)**

Current evidence on the safety and efficacy of the above forms of ablation (RFA) for atrial fibrillation in association with other cardiac surgery appears adequate to support the use of this procedure provided that the normal arrangements are in place for consent, audit and clinical governance.

### **IPG 84: High-intensity focused ultrasound (NICE, 2006)**

Current evidence on the safety and efficacy of high-intensity focused ultrasound (HIFU) for atrial fibrillation in association with other cardiac surgery is insufficient for this procedure to be used without special arrangements for consent and for audit or research.

## **AVJ catheter ablation (Pace & ablate)**

It was concluded that this technique was effective for patients with medically refractive paroxysmal AF, especially in the absence of any cardiac co morbidity.

## **Atrial defibrillators**

In the NICE guidance, this technology was considered to be useful in patients with recurrent persistent AF but not for those with paroxysmal AF. The HTA (Buxton et al) also published an updated review of the evidence and costs of implantable cardioverter defibrillators for arrhythmias in 2006. They concluded that ICD's could be useful for patients with ventricular arrhythmias, especially survivors of cardiac arrest and for those at risk of sudden cardiac death. They may also be useful for patients with heart failure and myocardial infarction. However, they confirmed that it was not possible to provide a robust estimate of long-term cost effectiveness of ICDs compared with amiodarone.

Although the NSF for Coronary Heart Disease recommends that all patients with symptomatic atrial fibrillation despite optimal medical therapy are referred to a rhythm specialist, it is not specific about optimum interventional treatment choices. The difficulty for commissioners is that there have been no clear guidelines about the relative costs and effectiveness of alternative invasive interventions. However, technologies used to support the interventions are developing at a rapid rate, the number of published trials and studies is increasing rapidly and the scientific understanding of the relationship between patient selection, energy sources, lesion sets and outcomes is constantly improving.

## **3.2 NATIONAL TARGETS**

It is a national target to improve mortality rates and increase the proportion of older people being supported to live in their own home by 1% annually in 2007 and 2008. In order to achieve these targets, it will be necessary for commissioners to seek more effective forms of treatment for AF. It is therefore incumbent on specialist service commissioners to work with cardiac networks and keep a track of the relative risk, costs and benefits of these procedures in comparison with standard drug therapy.

## 4. Objectives

The objectives of extending the availability of specialist interventional services for atrial fibrillation are as follows:

1. Reduce avoidable admissions for emergency care, investigations and cardioversion;
2. Increase NHS Trust elective capacity;
3. Prevent stroke;
4. Reduce the cost of medication in primary and secondary care;
5. Reduce the mortality and morbidity associated with drug treatments for AF;
6. Reduce the mortality and morbidity associated with drugs used in the prevention of stroke in patients with AF;
7. Advance performance against national public health targets, NSF and NICE guidelines; and
8. Reduce the burden of cost of AF for PCTs and the SCG to offset rising demands resulting from new standards and rising incidence rates.

## 5. Option Identification

There are three types of AF:

1. **Paroxysmal** – single or recurrent episodes of AF lasting for up to 7 days, which are self terminating
2. **Persistent** – single or recurrent episodes of AF lasting more than 7 days which are not self terminating (usually affects patients with structural or ischaemic heart disease and atrial disease tends to maintain AF once it occurs (Grubb, 2006))
3. **Permanent** – AF where cardioversion failed or was not attempted

This business case explores options for treating AF for patients during and after mitral valve surgery. More than 40% of patients referred for mitral valve surgery have continuous AF (Doukas et al, 2005) and many others have intermittent AF (Jeanmart, 2006).

If there are clear factors that have been causing AF, these are usually treated before treatment for AF is initiated. Following that, the treatment algorithms may differ for each type of AF, drawn from a choice of two treatment approaches:

1. Restore and maintain sinus **rhythm**
2. Allow AF to continue and ensure ventricular **rate** is controlled

The **Rhythm control** approach is geared to relieve symptoms, prevent embolism and avoid cardiomyopathy (Fuster et al, 2001). It involves the use of medication, electrical cardioversion and electrophysiological or surgical interventions to convert the abnormal cardiac rhythm associated with AF to normal cardiac rhythm.

Patients who have been successfully cardioverted are generally administered antiarrhythmic drugs for the long term to help prevent the recurrence of AF. The rhythm control strategy also requires the appropriate administration of antithrombotic therapy to reduce the risk of stroke and thromboembolic events occurring.

The **Rate control** approach is geared to minimise the symptoms associated with excessive heart rates (tachycardia) and prevent tachycardia-associated cardiomyopathy. It involves the use of chronotropic drugs or electrophysiological/surgical interventions to reduce the rapid heart rate (ventricular rate) often found in patients with AF. Although the atria continue to fibrillate with this strategy, it is nonetheless thought to be an effective treatment as it improves symptoms and reduces the risk of associated morbidity. However, the persistence of the arrhythmia continues the risk of stroke and thromboembolic events occurring. This risk is reduced by administering antithrombotic drugs.

Uncertainties remain about the most appropriate initial treatment strategy for individual patients (Fuster, 2001). NICE (2006) recommends that rate control should be the preferred approach in treating persistent AF for elderly patients without severe AF symptoms, patients with coronary artery disease and patients unsuitable for cardioversion or with contraindications to rhythm control drugs. Patients unsuitable for cardioversion include patients with mitral stenosis and patients with contra-indications to anti-coagulation drugs. However, rate control therapy often requires careful dose titration of combination drugs and is often initiated in the hospital setting. Some patients develop symptomatic bradycardia that requires permanent pacing.

NICE guidance indicates that rate control is suitable for patients with permanent AF, whereas rhythm control is indicated for patients with paroxysmal AF and patients with persistent AF who do not have the indications for rate control described above. However Grubb et al (2006) do not cite age as an indicator for rate control unless other indications are present i.e. structural heart disease; heart control is difficult at rest and exercise; or arrhythmia therapy fails and the consequences of AF and the risk of stroke persist.

## INDICATION FOR APPROACH TO THERAPY

Adapted from *Treatment Strategy Decision Tree* (NICE, 2006)

Approach	Paroxysmal AF	Persistent AF	Permanent AF
RATE	NO	YES	YES
RHYTHM	YES	YES	NO
Thromboprophylaxis	YES	YES	YES

Neither the rate control or rhythm control approaches to the conservative treatment of AF are effective in preventing strokes.

### 5.1 RHYTHM CONTROL OPTIONS

#### 1. Electrical Cardioversion +/- Drug Maintenance Therapy

Cardioversion is an intervention designed to restore the heart to normal rhythm in patients with persistent AF (Fuster et al, 2001). It can be achieved by means of drugs or by electric shocks applied through the chest wall using an external defibrillator. Current clinical practice regards electrical cardioversion (ECV) as the preferred strategy for treating prolonged persistent AF (NICE, 2006). It is usually an elective day case procedure carried out under general anaesthetic but it may also be carried out as an emergency procedure when the AF has resulted in heart failure, hypotension or worsened angina in patients with coronary artery disease. Anticoagulation therapy is initiated before the procedure to reduce the risk of thromboembolism.

AF is a chronic disorder and reoccurrence following a successful cardioversion is likely in most patients. Prophylactic treatment with anti-arrhythmic drugs is therefore indicated in patients with frequent or poorly tolerated paroxysmal AF and persistent AF (Fuster et al, 2001). UK clinical practice commonly uses Class 1c beta blockers or Class III anti-arrhythmic drugs to maintain sinus rhythm. Most maintenance drugs can be initiated in outpatients.

Since interventional procedures are indicated when conventional treatment has failed (NICE 2006), electrical cardioversion with maintenance therapy has been selected as the baseline comparator for interventional and surgical procedures.

#### 2. Interventional Cardiology

##### a. Internal Cardioverter Defibrillator (ICD)

Internal cardioversion with an implanted atrial defibrillator is a treatment option. However, the threshold of energy discharge required to achieve cardioversion is at a level uncomfortable to most patients. In addition, potential candidates, i.e. those with infrequent episodes of poorly tolerated AF, are usually also suitable for catheter ablation. NICE (2006) guidance states that this can be useful for patients with recurrent persistent AF and this option is therefore included in the option appraisal.

##### b. Pulmonary Vein Isolation

The recognition that foci triggering AF often originate in the pulmonary veins has led to ablation strategies that target this zone or electrically isolate the pulmonary veins from the left atria.

The procedure is performed by an electrophysiologist. Two catheters are passed into the right atria and two more into the left atria, the first is to map the pulse and the second is to deliver

radiofrequency energy. The left atria is entered through a transeptal puncture. Lesions are created outside all four pulmonary veins. The scars forming at the site of lesions created during the procedure (4-8 weeks later) block impulses firing from within the pulmonary veins. The procedure takes about 4-5 hours (Kusumoto, 2006).

From the evidence, NICE (2006) noted that patients resistant to pharmacological treatment, younger patients and those with lone AF may benefit from referral for PVI. Grubb (2006) reports that this option may be indicated for persistent or permanent AF. Kismet (2006) reports that although this procedure is usually used for paroxysmal AF with no structural disease in practice, it is also useful for persistent AF with structural disease. This option has therefore been selected for appraisal.

### **c. Bilateral atrial pacemakers**

Several studies have examined the use of atrial pacemakers to prevent recurrent paroxysmal AF. NICE found no evidence to specifically identify those patients with AF who have no other indication for pacemaker therapy for this treatment. This option has therefore been excluded from the option appraisal.

## **3. Surgical Ablation**

Cardiac ablation is a therapeutic method in which a form of energy is used to physically destroy a small section of damaged heart tissue that is a source of abnormal electrical activity causing or contributing to AF. NICE (2006) guidance recommended that patients undergoing concomitant cardiac surgery (eg mitral valve surgery) could be considered for surgical ablation for AF.

The Society of Cardiothoracic Surgeons (2006) however, suggest that some patients are so troubled by the way they feel when they are in atrial fibrillation or by the medications they must take that a surgical option is appropriate. In addition, they also state that individuals in atrial fibrillation who have experienced a stroke and are at significant risk of another stroke may be indicated for surgery.

### **a. Maze**

Based on mapping studies of human and animal AF, Cox developed a highly successful surgical procedure in the mid 1980's, during which incisions are made in the right and left atria to confine electrical impulses to defined pathways to reach the AV nodes. This 60 minute procedure is carried out through a median sternotomy and involves cardiopulmonary bypass. Patients are usually in hospital for 5-7 days, including 1-2 days in an intensive care unit.

The Maze is the only procedure that addresses all three adverse consequences of AF: Irregular rhythm; risk of thromboembolism and loss of atrioventricular synchronization. Although the effectiveness of the procedure is widely accepted (Chiappini, 2004), because it is technically demanding, time consuming and requires cardiopulmonary bypass (Song and Puskas 2004, Chiappini 2004) it has not been widely adopted. Therefore, efforts are being made to find alternative means of creating full-thickness continuous linear incisions that preclude the ability of the atria to fibrillate. This option has been excluded from the appraisal on the basis of persistent low adoption in the UK and the potentially high demands on hospital resources.

### **b. Modified Maze**

During the modified Maze procedure, lesions and scar tissue are created by ablation using either radiofrequency, cryotherapy, microwave, ultrasound or laser energy sources to block abnormal impulses and promote normal impulses through the proper pathway. There is little standardization in the pattern of these lesions which may include isolation of pulmonary veins, excision of left or both atrial appendage, excision of left or both atria and lesions on the proximal bundle of His. The procedure can be minimally invasive but is most commonly an open procedure in the UK. Open operating time in experienced hands is around 15-20 minutes and the patient requires an average stay in hospital of 2-3 days, including 1 day in intensive care.

Khargi et al (2005) carried out a systematic review of success rates of traditional cut and sew methods of surgery with radiofrequency, cryotherapy and microwave energy sources and found no difference in post operative conversion rates after confounding variables had been taken into account. There is a NICE IPG (2005) covering each of radiofrequency, microwave and cryoablation, which review randomized controlled trials on the first two. The NICE IPG (2006) covering ultrasound ablation describes only one case series report.

In the interests of standardization and based on the widest availability of data, the Modified Maze using radiofrequency ablation (specifically including pulmonary vein isolation and ablation of the left atria and the left atrial appendage +/- ablation of the right atria and right atrial appendage) has been selected as the surgical option for the option appraisal. This pattern of lesions appears to give consistently better results in the literature. In contrast to the Maze procedure, intra-operative radiofrequency ablation obviates the need for a heart-lung machine, requires less operating time, requires shorter bed stay and reduces damage to heart tissue and scarring to the heart.

## **5.2 RATE CONTROL OPTIONS**

### **1. Drug Maintenance Therapy**

In rate control therapy the patient is left in AF, provided that the rate of ventricular contractions is in good control, the output of blood from the heart is adequate and their blood is adequately thinned by Warfarin to prevent strokes. Heart rate is controlled using beta-blockers or calcium channel blockers. Beta blockers are included in the option appraisal.

### **2. Interventional Cardiology**

#### **a. Ventricular pacemaker implantation**

Ventricular pacing may be used as a strategy to reduce the irregularity of the ventricular rhythm (Clark et al, 1997). This modality may be useful for patients with marked variability in ventricular rates and for those who develop resting bradycardia during treatment with medications prescribed to control rapid ventricular rates with exertion (Fuster et al, 2001). NICE guidance (2006) recommends that pacemaker therapy in AF may be indicated for symptomatic low heart rates. Ventricular pacing is an adjunct to other treatment options and is dealt with as an “effect” of other treatment options in the appraisal.

#### **b. Ventricular pacemaker & atrioventricular (AV) nodal ablation**

The procedure is performed by an electrophysiologist. A catheter is inserted through a vein in the groin and guided to heart. Radiofrequency ablation is carried out on the atrioventricular (AV) node. This procedure permanently slows the heart rate and a permanent pacemaker is required. NICE (2006) concluded that atrio-ventricular node ablation was effective for patients with medically refractive paroxysmal AF, especially in the absence of any cardiac co morbidity. It is obviously also useful for patients with AF who have a rapid ventricular rate. This option is therefore included in the option appraisal.

**Treatment options selected for appraisal include:**

1. **Electrical cardioversion +/- arrhythmia drug maintenance therapy**
2. **Rate control medication**
3. **ICD**
4. **Pulmonary vein isolation**
5. **Radiofrequency modified Maze**
6. **Pace & ablate**

**The following evaluation of these treatment options should be read in the context of the treatment algorithm in Appendix 1, since not all of the options are indicated for all types of AF**

## **6. Option Appraisal**

Whilst the treatment algorithms may differ for each type of AF, the goals of treatment for AF remain consistent:

### **GOALS OF TREATMENT FOR ATRIAL FIBRILLATION**

1. **Reversing the risk factors that cause atrial fibrillation**
2. **Slow the heart rate**
3. **Prevent strokes**
4. **Convert AF to normal heart rhythm**
5. **Prevent recurrence**

*Lee (2006)*

These goals are used as parameters for appraising invasive treatment options along with risk and cost impact. As a baseline comparator for invasive treatment options, the success of conventional treatments is outlined below:

### **6.1 OUTCOMES OF CARADIOVERSION & MAINTENANCE THERAPY**

Electrical cardioversion carries a risk of thromboembolism. The success rate after 3 days is 86% but only 23% of patients remain in sinus rhythm after one year and 16% after two years (Fuster, 2001). Repeated cardioversion after a relapse results in 40% sinus rhythm at 1 year and 33% at two years (Fuster, 2001). After a third cardioversion, 54% achieve sinus rhythm at one year and 41% at two years (Fuster, 2001). Therefore successive cardioversion will restore normal rhythm in a substantial proportion of patients but relapse rates are high without concomitant antiarrhythmic drug therapy. Prophylactic treatment with antiarrhythmic drugs is therefore indicated in patients with frequent or poorly tolerated paroxysmal AF and persistent AF (Fuster, 2001). In one study, arrhythmia free survival over 4 years was 30% for patients on maintenance therapy and less than 10% for patients on no maintenance therapy following cardioversion (Van Gelder et al, 1996). UK clinical practice commonly uses Class Ic beta-blockers or Class III antiarrhythmic drugs to maintain sinus rhythm.

Effective maintenance of sinus rhythm is known to improve overall function and mortality. For example, In the AFFIRM trial, significant improvements in mental and physical health scales and exercise tolerance were noted in patients previously diagnosed with AF and who had attained and maintained sinus rhythm as a result of drug treatment. The level of improvement in a highly symptomatic group of patients was between 20-40% (Kusumoto, 2006). In addition, the AFFIRM trial showed that patients on treatment for AF with sinus rhythm had a 47% reduction in mortality compared to those with AF, but this benefit was offset by the increased risk of mortality from Digoxin or anti-arrhythmic drug use (30-50% increase in mortality) (Corley et al, 2004). The effectiveness of anti-arrhythmic drugs is known to diminish over time i.e. 50% failure at one year and 84% failure at 2 years (Ezekowitz, 2003 and Lundstrom 1998). Similarly, the prospect of spontaneous return to sinus rhythm diminishes because of maladaptive changes that occur in the atrial tissue, known as electrical remodeling.

These factors limit the role and efficacy of anti-arrhythmic drugs in the maintenance of normal heart rhythm. For example, in the AFFIRM trial, 46% of patients receiving amiodarone were in sinus rhythm compared to a 30% incidence in the placebo arm, so the absolute benefit of amiodarone was only 16% (Corley et al, 2004). In addition, antiarrhythmic medications are associated with significant and possibly lethal side effects. In the AFFIRM trial 12.3%, 11.1%, and 28.1% of patients taking amiodarone, sotalol and Class I antiarrhythmic medications respectively had to discontinue the drug within 1 year of initiating therapy due to side-effects (Corley et al, 2004).

**The effectiveness of cardioversion reduces over time  
The effectiveness of rhythm control drugs reduces over time  
Digoxin or anti-arrhythmic drugs are associated with a 30-50% increase in mortality (Corley et al, 2004)**

## 6.2 CONSERVATIVE TREATMENTS FOR RATE CONTROL

An alternative to maintaining sinus rhythm in patients with Paroxysmal or Persistent AF is to control ventricular rate. A randomised trial failed to show any difference in outcome between the two approaches, except that rhythm control produced better exercise tolerance (Hohnloser, 1998). However, the results of further studies are pending. The rate control drugs require careful titration and some patients develop symptomatic bradycardia and require pacing. The results of the AFFIRM trial emphasised that a rate control strategy is appropriate for many patients, particularly those that are minimally symptomatic (Corley, 2004). Grubb (2006) describes the indications for rate control as the presence of substantial structural heart disease; when the rhythm control strategy has failed but the risk of stroke and consequences of AF persist or when heart control is difficult at rest and exercise.

**Rate control drugs and rhythm control drugs produce similar outcomes**

## 6.3 PREVENTION OF BLOOD CLOTS AND STROKE

NICE (2006) recommends that all patients with AF should receive anticoagulants. The choice between Asparin and Warfarin depends on stratified risk. Warfarin is recommended for those patients at high risk and would therefore be the most likely preventative drug of choice for patients considered as suitable for surgery.

Studies show that 1000 patients treated with Warfarin prevents 30 strokes and 7 deaths at a cost of 7 major bleeding episodes per annum (Sudlow et al, 1998). According to the NICE CG36 Costing Report (2006),

26% of all AF patients should be receiving Warfarin treatment but are not getting it now. If all patients who could benefit were receiving it, this would be a significant additional cost burden for the PCT's (£36m across England). However, NICE estimates that £55.3 million could be saved against the cost of treating avoidable strokes. Although this is partially off set by the additional cost of treating bleeding problems resulting from Warfarin therapy, the net saving is calculated to be almost £46m.

**Anticoagulation is recommended by NICE for AF patients on anti-arrhythmic or rate control drugs in order to prevent stroke**

**Under provision means this could present a huge short term cost burden to the NHS**

#### **5.4 APPRAISAL SUMMARY OF INVASIVE INTERVENTIONS**

NICE recommends that interventional procedures are considered after medication has failed but does not compare and contrast procedures. The table in Appendix 2 compares how well each treatment option meets the treatment goals for AF along with consideration of risk and relative cost. Relative costs are taken from the Trust's AF financial impact model.

Cardioverters with atrial cardioversion and ventricular pacing capabilities provide an effective but painful treatment for AF and suit patients who have infrequent but poorly tolerated episodes of AF. However, these patients are also suitable for catheter ablation and this is usually the preferred option. Patients implanted with ICD's require ongoing maintenance therapy and anticoagulation and there is some evidence to suggest that drug use increases following implantation (Connelly et al, 2000). Whether this is due to the effect of the procedure or to incidental deterioration of the AF is unclear. As a result, the modeled overall cost of treatment for this option is high (Appendix 3).

Of the two types of catheter ablation, the pace and ablate option is low in cost and appears to be effective in reducing the healthcare costs associated with treating AF (Appendix 2). However, there is a high risk of developing permanent AF (24% - NICE, 2006) and this may mean that the reduction in healthcare utilization observed in Lee et al's study is not reproducible in subsequent years and the model may therefore underestimate the true cost of this option (Appendix 3). The Cleveland Clinic (2006) do not see this as a standard first line option and although NICE (2006) do recommend it for persistent AF, this is contingent on the absence of cardiac morbidity. This may therefore exclude patients with mitral valve stenosis. In addition, pulmonary vein isolation is the preferred option for paroxysmal AF unless the patient is unsuitable.

Pulmonary vein isolation has a good initial success rate and relatively low risks. There is some evidence that this procedure reduces the risk of stroke and healthcare utilization (Appendix 2). However, reoccurrence of atrial fibrillation is high and the success rate for the procedure is lower for patients with mitral valve stenosis (Appendix 2).

The radiofrequency modified Maze procedure as a concomitant procedure with mitral valve surgery is the only option that may address all 5 goals of treatment for AF (Appendix 2). The procedure has good success rates which appear to be durable over time e.g. the success rate was reported by Sie *et al.* as 90% at one year, 86% at two years and 75% at three years and Patwardhan et al (2003) reported the rate of attrition to be 8.33 % over a two year follow up. The overall cost of treatment is comparable to pulmonary vein isolation (Appendix 3). The procedure is quick and complication rates and length of hospitalisation are comparable with mitral valve surgery alone (Appendix 2). There is some indication that the procedure may reduce hospital admissions and strokes (Appendix 2). The effect seems to be durable for most patients (Appendix 2).

## **7. Preferred Option**

For eligible, consenting patients, the concomitant radiofrequency modified Maze procedure is the preferred invasive treatment option. Published data suggests it delivers:

- A high cure rate of atrial fibrillation (Chiappini et al, 2001)
- A reduced chance for blood clots and stroke, by removal of the left atrial appendage (Benussi et al, 2002)
- Fewer or no symptoms related to abnormal heart rhythms (Deneke et al, 2002)
- Less or no reliance on blood thinners such as Coumadin (Jeanmart et al, 2006)
- Less or no reliance on anti-arrhythmic drugs such as Amiodarone (Doukas et al, 2005)
- Some patients who have had the procedure report an ability to exercise more frequently and for longer periods of time (University of Chicago, 2006)
- In some cases, the procedure will reduce the size of the atria, therefore lessening the risk for other complications, such as heart failure (University of Chicago, 2006)

After four years experience of concomitant radiofrequency ablation, Martin-Suarez et al (2006) concluded that the only predictive factor for failure of the procedure was low ejection fraction. Ejection fraction is a measure of the ability of the left ventricle to pump blood into the system. A low ejection fraction is a sign of congestive heart failure. They found no evidence that patients should be contra-indicated on the basis of age, dimensions of the left atria, duration of symptomatic disease or previous operation. They found the bipolar method or endocardial monopolar most successful, whilst the epicardial monopolar was least successful.

## **8. Benefits**

### **8.1 NUMBER OF ADMISSIONS FOR EMERGENCY CARE, INVESTIGATIONS AND CARディオVERSION**

In Raman et al's study (2003), only 3 out of 16 (20%) patients required defibrillation in the first three months following concomitant radiofrequency ablation and then remained in sinus rhythm. This contrasts with Lee et al's (1998) data on number of admissions per annum before surgery e.g. 2.6 times per annum. Subtract from this the reported frequency of strokes and bleeding complications and this gives some indication of the number of cardioversions that might have been required by eligible patients on drug treatments alone.

There is also evidence to suggest that admissions for stroke and anticoagulated bleeding events would reduce, creating additional bed capacity.

### **8.2 NHS TRUST ELECTIVE CAPACITY**

The concomitant radiofrequency modified Maze procedure requires around 20 minutes more operating time than the mitral valve surgery alone and does not increase overall length of stay or time in ICU. This compares to catheter based procedures such as AV node ablation and insertion of a pacemaker, which takes just less than an hour, and pulmonary vein isolation which takes 4-5 hours. These take up considerable electrophysiologist and procedure room time.

### **8.3 STROKE**

Benussi et al (2002) reported that 98% of patients were free from stroke at three years. Bando et al (2002) reported that only 79% of patients were free from stroke following mitral valve repair alone. Handa et al (1999) reported a reduction in stroke and anticoagulated related bleeding events following surgery.

### **8.4 COST OF MEDICATION IN PRIMARY AND SECONDARY CARE**

In Chiappini's meta analysis the success rate of surgery was 76.3%. Doukas et al (2005) reported that all patients had anti-arrhythmic or rate control drugs post operatively but that none of the patients in sinus rhythm needed them at 12 months. Gillinov et al (2002) report that 30-40% of patients leave hospital in AF but most are restored to sinus rhythm within three months. Although there is no published cost data, this infers that significant cost savings can be made against medication costs. In addition, whilst most patients are given anticoagulation therapy pre and post operatively to mitigate for surgical risk, Jeanmart et al (2006) reported that only 50% of patients were given ongoing anticoagulants after the initial three months. In this study the left and right atrial appendages were removed.

### **8.5 MORTALITY AND MORBIDITY ASSOCIATED WITH DRUG TREATMENTS FOR AF & DRUGS USED IN THE PREVENTION OF STROKE**

Chiappini et al (2004) reported a hospital mortality rate of 2.7% and Sie et al (2004) reported a hospital stroke rate of 1.4%. For all patients, the 30-day mortality rate was 2.5% (70% confidence limits 1.6% to 3.4%) in Chua et al's case review (1994). Chua et al (1994) concluded that concomitant surgery carries negligible morbidity with no adverse effects on operative mortality compared to mitral valve surgery alone. Patwardhan et al (2004) also found that mortality and morbidity were comparable between concomitant surgery and mitral valve surgery alone.

### **8.6 PERFORMANCE AGAINST NATIONAL PUBLIC HEALTH TARGETS, NSF AND NICE GUIDELINES**

Provision of concomitant RF modified Maze during mitral valve surgery for patients with AF meets NICE CG-36 and the NICE IPG on Radiofrequency ablation for AF as an associated procedure with other cardiac surgery. Since there is some evidence that the procedure reduces the risk of stroke and dependence on anti-arrhythmic drugs and anti-coagulants, it is likely that increased provision will contribute to NHS health gain targets by having a beneficial effect on mortality and the number of older people able to continue living in their own homes.

### **8.7 FINANCIAL IMPACT**

Although surgery is costly in the first year, the success rate of surgery is high and there is some direct evidence to support that this will reduce dependence on anti-arrhythmic drugs and anti-coagulants and since stroke rates seem to be reduced, the rate of hospitalisation should also reduce (see above). The Trust's predictive model shows that the relative five year treatment costs for the concomitant procedure are lower than for all other treatment alternatives except ablation of the AV node. Since this is not a widely adopted procedure, it is likely that increased adoption of the concomitant modified Maze will have a beneficial effect on overall healthcare costs.

### **8.9 SURVIVAL**

In Chiappini et al's meta-analysis (2004) overall survival after surgery was 97.1%. 1 year survival and 5 year survival following surgery were reported to be 95% and 87.8% respectively (Izumoto et al, 2000). This compares to a 5 year survival rate of 76% for patients with AF following mitral valve surgery alone (Chua et al, 1994)

## 9. Risks

In Chiappini et al's (2004) meta analysis of six studies, with a total of 451 patients, there were 12 (2.7%) hospital deaths. The nonfatal hospital complications were repeat thoracotomy (19), low cardiac output requiring an intraaortic balloon pump (7), sternal wound infection (2), pneumothorax (2), endocarditis (1), stroke (1), and gastrointestinal bleeding (1). No severe arrhythmias were observed postoperatively, and 4 (0.8%) patients required implantation of a dual-chamber pacemaker.

The results of Doukas et al's (2005) randomized double blind trial comparing mitral valve surgery alone with concomitant radiofrequency ablation showed that 4.4% of radiofrequency ablation patients had a pacemaker at 12 months compared with 9.1% of controls. Doukas et al (2005), Chua et al (1994) and Patwardhan et al (2004) found that mortality and morbidity were comparable between concomitant surgery and mitral valve surgery alone.

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## Glossary

### Atrial fibrillation

When the atrium (the upper, low pressure chamber of the heart) does not squeeze or contract at one uniform, coordinated time but instead contracts irregularly with one portion contracting well before or after another, the result is atrial fibrillation. When this happens, the atrium cannot push blood into the ventricles in the normal manner.

### Atrioventricular Node

Although the upper chambers (the atria) and the lower chambers (the ventricles) are physically connected to one another to allow blood to flow from one to the other, from an electrical standpoint, they are normally connected to one another at only one point. This point is called the atrioventricular node. Therefore, the electrical impulse from the atrium must pass through this point to reach the ventricle. If this connection is destroyed, for example in the cardiac catheterization lab by radiofrequency ablation ("A-V node ablation"), the electrical impulse from the atrium can no longer reach the ventricle. Regardless of what is going on in the atrium electrically- [sinus rhythm](#), atrial flutter, or [atrial fibrillation](#)-the ventricle will beat at its own pace. In some individuals, there is an extra or "accessory" pathway from the atria to the ventricles, which results in a syndrome causing palpitations and a rapid heart rate called "Wolfe-Parkinson-White syndrome."

### Cardiac catheterization

Cardiac catheterization is a procedure accomplished by passing small tubes or catheters into the heart from arteries and veins in the groin or arm. It is performed by a cardiologist with specialized training. Many conditions affecting the heart require direct measurement of pressures in the chambers or injection of dye (contrast material visible on Xray).

### Coronary artery disease

Coronary artery disease is characterized by a narrowing or "[stenosis](#)" of the blood vessels to the heart resulting in inadequate blood flow to the heart muscle itself.

### Heart failure

Heart failure is a degenerative condition that occurs when the heart muscle weakens and the ventricle no longer contracts normally. The heart can then no longer pump enough blood to the body. This may limit exercise tolerance, or may cause fluid retention with swelling of the feet or shortness of breath.

### Ischemic heart disease

When the arteries providing blood to the heart, the coronary arteries, become

clogged the heart cannot get enough oxygen and nutrients. It then becomes "ischemic." This condition is called ischemic heart disease, and it is caused by coronary artery disease.

### Median sternotomy

The incision traditionally used to perform heart surgery in which the sternum or breastbone is divided down the middle from top to bottom.

### Minimally invasive heart surgery

The term minimally invasive heart surgery is used to describe a variety of approaches that reduce the trauma of surgery and speed recovery. These approaches include "keyhole" surgery, and heart surgery without the use of a heart lung machine, and many other techniques.

### Mitral valve

There are four valves in the heart, two on the left side and two on the right side. On each side there is an inflow valve to the ventricle - the main pumping chamber - and an outflow valve. The mitral valve is the inflow valve for the left ventricle. As such, it closes when the ventricle squeezes blood out to the body, and then opens to let more blood into the ventricle.

### Stenosis

Narrowing of a valve or an artery is called stenosis. A stenotic valve does not open completely and therefore it obstructs or blocks blood from moving through it normally. An artery can become stenotic as well, such that there is obstruction of blood flow through it to the organs of the body.

### Sinoatrial node

The normal "pacemaker" for the heart is an area of specialized cells in the [atrium](#) called the sinoatrial or "SA" node. These cells automatically send out an electrical impulse to the rest of the heart telling it to contract.

### Sinus rhythm

The normal rhythm of the heart originates in the [sinoatrial node](#). It is called sinus rhythm.

### Ventricle

The main pumping chamber of the heart is the ventricle.

### Ventricular function

The performance or strength of the main pumping chamber of the heart is called "ventricular function."



# THE ASSESSMENT OF ISCHAEMIC HEART DISEASE

**Mr. S. Rooney, Mr. G. Cooper and Mr. M. Lewis**

## **Objective:**

At the end of this session, participants should be able to demonstrate knowledge and understanding of the preoperative evaluation of patients undergoing surgery for ischaemic heart disease.

The following aspects of patient assessment will be considered.

History  
Examination  
Troponin  
ECG  
Exercise Stress Test  
Positron Emission Tomography  
Dobutamine Stress Echo/MRI  
Coronary angiography.

The format of the session will be that of case based discussion. Scenarios will be considered and investigations reviewed. Indications and contraindications for surgery will be examined to allow treatment plans to be formulated.

The following textbooks/websites may prove useful reading:

The ECG Made Easy. Hampton J.R., Churchill Livingstone  
A concise introduction to the ECG.

Measurements in Cardiology. Edited by Peter Sutton, Parthenon Publishing.  
Good chapters on ECG (including X-tests), Echo, Cardiac Catheterisation and Nuclear Cardiology.

[www.cardiologysite.com](http://www.cardiologysite.com)

A useful website that introduces the concepts of angiography including a helpful description of the views used to image the coronaries.

<http://info.med.yale.edu/intmed/cardio/imaging/contents.html>

Clear site, with many images available. Very good 3D viewer demonstrating relation of structures from different viewing angles. (Look in the "Heart in Radiographs" section).

<http://heart.bmj.com/collections/index.dtl>

Excellent collection of review articles on a wide selection of topics that may come up in the exam.



## CARDIOPULMONARY BYPASS

**Mr. I. Wilson, Mr. R. Gohil, and Dr. D. Green, Dr. P. Townsend -**

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

Taylor K M. Cardiopulmonary Bypass in Seminars in Thoracic and Cardiovascular Surgery 1990.2:291-415

Taylor K M. Cardiopulmonary Bypass. Principles and Management. Williams and Wilkins 1986

Utey J R. Pathophysiology and Techniques of Cardiopulmonary Bypass Vol I and Vol II Williams and Wilkins 1982/1983

## NOTES

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