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CARDIOPULSE

ESC/EACTS Guidelines on the management of valvular heart disease

Cardiologists and surgeons have joined forces to write the Valve Guidelines for the first time

The 2012 Guidelines on the Management of Valvular Heart Disease are a joint effort between the European Society of Cardiology (ESC) and the European Association for Cardio-Thoracic Surgery (EACTS). It is the first time the two organizations have partnered on valves and follows a previous collaboration on Guidelines for myocardial revascularization.

But, there was a minimal amount of major opposition between the two groups. 'They were pretty much on the same line for most of the document', says Professor Alec Vahanian (France), who co-chaired the Guidelines Task Force with Professor Ottavio Alfieri (Italy). 'It was quite surprising and probably reflects the fact that the whole team spirit has been [at play in valves] for a while, at least in Europe'.

The most controversial area was how to manage asymptomatic patients, especially those with aortic stenosis and regurgitation.

The Guidelines will be published in *European Heart Journal* and *European Journal of Cardio-Thoracic Surgery* and presented for the first time during the ESC Congress in August 2012 in Munich. They contain a number of new elements since the last ESC Guidelines were published in 2007.

The fact that they are joint guidelines is one of the most important changes, says Vahanian. Traditionally, in the field of heart disease, surgeons and cardiologists cooperated, but there was always one 'gatekeeper' and one 'follower'. Today, the two groups collaborate, working hand in hand as a team. The change is largely down to the advent of the transcatheter aortic valve implantation (TAVI) procedure.

Alec Vahanian

It was felt that writing joint guidelines would be a good reflection of the heart team's importance. But that only covers the theoretical aspect. Practically, Vahanian says that in previous years, European surgeons have not always been aware of the ESC Guidelines on valves and often quoted American guidelines instead. 'We hope that they will recognise and implement these guidelines', he says.

The table of contents mirrors the 2007 document, starting with an introductory chapter. A chapter for general comments follows and here the emphasis is risk stratification evaluation. Next are chapters covering each specific valve disease: aortic regurgitation, aortic stenosis, mitral regurgitation, mitral stenosis, and tricuspid disease. The remaining chapters are: combined and multiple valve diseases; management of patients with prosthetic valves; management during non-cardiac surgery; and management during pregnancy. The latter two chapters are very short because they are cross-linked with recent ESC Guidelines on these topics.

The Task Force has done its best to keep the document short. It has avoided listing thousands of references; for this detail, readers can go to the ESC Textbook.

The field of valves still has very few trials, but a few large studies and randomized trials have been done. Evidence is Level C at best, which means that guidelines largely rely on expert consensus. Much discussion is involved, particularly when different communities are around the table.

There have been developments in the last 5 years. There is now a sizeable amount of data on patient evaluation and risk stratification in both surgical and interventional procedures, and this has been given more weight in the new guidelines.

Progress has also been made in imaging, primarily in echocardiography and stress echocardiography. Other areas of imaging are touched on, including the role of multislice computed tomography and magnetic resonance imaging which have an increasing role to play in valve disease because of TAVI. The new recommendations from the European Association of Echocardiography on the quantification of valve stenosis and valve regurgitation are also quoted.

In terms of therapeutic options, more data have been accumulated on valve repair. The key new feature is TAVI and to a lesser degree percutaneous edge-to-edge valve repair. The Guidelines include a strong recommendation about where TAVI should be performed and proposes indications and contraindications for the technique. Technical issues relating to TAVI are not described in detail, as these were covered in the ESC and EACTS

recommendations on the TAVI procedure in 2008. The guidelines also highlight therapies that have been shown not to work, such as medical treatment in aortic stenosis.

The Euro Heart Survey and several registries in the USA have shown that simple, straightforward things are not being done and the Guidelines propose a step-by-step approach for decision-making. Vahanian hopes that the Guidelines will act as an incentive to implement a heart team discussion where this does not already occur.

More data are being collected on valves and it i's possible that the field would not always be plagued by a lack of evidence. New techniques are more extensively evaluated; e.g. TAVI is just 10 years old and already there are at least two randomized studies.

So while the field of valves will never see trials in thousands of patients to evaluate one prosthesis vs. another, the approach to research is changing. Vahanian predicts that more and more randomized studies will be conducted, helping to accumulate better evidence in this controversial field.

Jennifer Taylor, MPhil

How cost-effective are drugs and devices used in cardiology?

The first of four feature stories on cost-effectiveness in medicine is this introduction by Dr J. Jaime Caro. The remaining stories will follow in consecutive issues of CardioPulse

J. Jamie Caro

On the face of it, this seems to be a very reasonable question to ask and one that, by now, we should be able to readily answer. Indeed, the number of papers mentioning cost-effectiveness in the European Heart Journal in the first 6 months of 2012 equals that of the entire decade of the 1980s—and back then, papers simply mentioned it; none was based on actual analysis. It turns out that despite the much increased attention, this remains a very difficult question to address.

'Cost-effectiveness' is a term that has come to be loosely applied in medicine to various types of economic analyses whose common ground is that they evaluate the efficiency of an intervention. This efficiency is conventionally computed as the increased monetary outlay per unit gain in health, the latter being quantified often in quality-adjusted life years (QALYs). Although this inverse measure is somewhat awkward in that a higher number means less cost-effectiveness and a lower one means more, it has been widely adopted by those who do research in this area.

A more difficult problem is that we are not sure what exactly it means to be 'cost-effective' because this requires some judgment about what is a reasonable maximum payment for a unit of health gain; and this is exceedingly difficult to establish on the basis of evidence. Some jurisdictions have simply set a threshold (per QALY gained) to operate by, without providing any strong basis for it (e.g. £30 000 in the UK, $50 000 in the USA), whereas others propose a range (e.g. up to €80 000 in the Netherlands) and many avoid the issue entirely (e.g. France and Germany). The WHO has proposed that every country use a threshold of three-fold its per capita GDP, which would put the USA around Int$150 000, the Dutch close behind and the UK closer to the EU average of around Int$100 000. With such variations in the meaning of 'cost-effective', it seems clear that it is a fool's errand to try to state whether cardiovascular interventions are cost-effective, in absolute terms.

Nevertheless, it is possible to peruse a database such as the Cost-Effectiveness Analysis Registry maintained at Tufts University (https://research.tufts-nemc.org/cear4/) and get some idea of where cardiovascular interventions lie, compared with other broad categories. At first glance, it appears that the estimates are all over the place with some claiming savings while others state that the intervention increased costs with no additional benefits. In between, the values range from below US$1000/QALY to hundreds of thousands of dollars. This is not surprising, given that the cost-effectiveness ratio is highly sensitive not only to the effectiveness and cost of the intervention in question but also to the context of the analysis (when, where, country, health care system, and so on), the comparison addressed (much easier to get a low ratio when comparing with no treatment than when comparing with another intervention in the same class), the population at issue, and the methods used to estimate the ratio (e.g. how the costs are computed, how health gains are projected and for how long, the sources of evidence, etc.). In the face of such variability, one might be tempted to abandon the quest.

However, on closer inspection, patterns seem to emerge. Firstly, few of the analyses are about medicines and those that are, tend to look at highly specific populations (e.g. rosuvastatin in 66-year-old patients with hs-C-reactive protein $>$2.0 mg/L, LDL-C$<$130 mg/dL, Framingham risk score of $>$10%, with no history of

cardiovascular events and who are never users of statins). Nevertheless, cardiology continues to be the most common arena for economic analyses of conventional pharmaceuticals, according to a recent review of this Registry (http://dx.doi.org/10.4161/mabs.4.2.18812). Secondly, the estimates from most of those about medicines tend to fall below any of the thresholds, whereas those about devices tend to be higher, even above the thresholds. It is unclear whether this (highly unscientific!) impression—borne out by the three most recent cost-effectiveness papers in the Journal—result from inherent differences among these types of interventions (unlikely) or rather from the less mature methodology on the device side (more likely).

If we cannot meaningfully answer the question in absolute terms, can we at least do so by comparison with other therapeutic areas; that is, how cost-effective are interventions in cardiology relative to those, say, in diabetology or in pneumatology? Perusal of the same Tufts registry reveals that in both chronic obstructive pulmonary disease and diabetes, most of the analyses are about medicines (not surprising, given the relative paucity of devices in those areas) and the results also vary considerably. That said, the cost-effectiveness ratios tend to be higher than those for medicines in cardiology, particularly for chronic obstructive pulmonary disease. This probably reflects the small incremental gains obtained with anti-diabetic agents and the lack of strongly effective interventions in chronic obstructive pulmonary disease. Of course, the impression left by this unsystematic relative assessment—even if it had been confirmed by a proper, full-on analysis—would not have much of an implication because no health care system would allocate resources on the basis of comparisons of efficiency across therapeutic areas!

So where does this leave us? A cynic would say 'nowhere much'—and I am hard pressed not to be that cynic—but perhaps it indicates that the proper role of cost-effectiveness in health care decisions has yet to be fully understood. The result is an immature approach with a bewildering array of analyses leading to unclear implications and an underfunded field of methodological research. This may have been acceptable in the past, but as societies face the reality of having to restrict access to devices and drugs with proven efficacy, perhaps this will no longer be considered 'good enough'.

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Medical innovations, budgets, and cost-cutting

Health care budgets long facing financial pressures have come under yet more scrutiny in the current economic climate. Emma Wilkinson investigates whether cost-cutting is stifling innovation and the adoption of novel therapies across Europe

Health care is an expensive commodity and novel therapies, by their very nature, are particularly costly. In an era of increasing elderly populations and lifestyle-associated diseases, health systems, be they social or private, must place limits on how money is spent. Yet some clinicians warn that this is happening at the expense of innovation. That is, they are not permitted to use novel therapies—even when they are widely and successfully being used elsewhere—because of an over-cautious approach.

Antonio Colombo

Prof. Antonio Colombo, chief of invasive cardiology at San Raffaele Hospital in Milan, says that there is no specific funding for innovations in Italy and like many other countries in Europe, cardiologists are limited to carrying out those procedures paid for by the national health service. 'If it's not approved that's it, the patient cannot have it, unless they pay for it themselves in a private hospital, which is rare', he explains.

Italy is behind France and Germany in implementing new devices he says, and he and his colleagues have to spend a lot more effort than some of their European counterparts on encouraging the adoption of new medicines and technology. The current process of approving therapies is stifling slow, he adds, which in turn dissuades companies from investing in the necessary clinical trials. 'There should be a board which evaluates important innovations and a fund set aside for some leading institutions to then make a decision on which of those procedures they want to do. This way, there would still be a limit on what could be spent but there would be some access'.

Dan Atar

Freek W.A. Verheugt

However, Prof. Dan Atar, head of cardiology at Oslo University Hospital Ullevå in Norway, says: 'If Italy is slow, we are very slow'. He explains that Norway too has a national committee to assess new procedures, who are very stringent in their standards. 'The best example is TAVI – percutaneous replacement of aortic valves – where countries such as Germany have done thousands of procedures but we are still in the process of evaluating this. Another example is the new oral anticoagulants to replace Warfarin – the medicines agency has been extremely reluctant. We have data which is excellent but approval is very very slow because it's about saving money'. Cardiologists have had some success lobbying the government when they really believe a therapy should be adopted—as happened with novel antiplatelet agents in MI—but he describes his health system as 'over-cautious' and under 'very high levels of scrutiny'.

He does believe the politicians have a 'plausible argument' for restricting novel therapies which go hand in hand with higher expenditure, when health care budgets can easily spiral out of control. However, one change he would like to see is a longer term view of cost-effectiveness rather than the '1 year' health budget on which decisions are currently made.

Piotr Ponikowski

Caution in adopting new technologies is seemingly a common complaint from cardiologists around Europe. In Poland, says Prof. Piotr Ponikowski, head of heart diseases at Wroclaw Medical University, the health service is 'too little reluctant' to take up innovation. 'For example, the MitraClip – other countries are doing a lot of procedures with this device but in Poland it is not reimbursed. We do some novel things but not on such a big scale as other countries'.

His hospitals are using the MitraClip in some cases because the clinicians pushed the director to provide funding, but in general, clinicians face a barrier in that the agency that decides what procedures will be reimbursed are meticulous in wanting to see a large amount of evidence before approval. Prof. Freek Verheugt, at the Heart Center, Onze Lieve Vrouwe Gasthuis, Amsterdam, says that in the Netherlands, cardiologists tend to wait for updated guidelines before using new therapies but that uptake of devices is usually much faster 'because the industry presses much harder'.

Even for those countries at the forefront of adopting new therapies, there are still financial controls, says Dr Giovanni Pedrazzini, deputy chief of cardiology at Cardiocentro Ticino in Lugano, Switzerland. 'Swiss centres are very fast in adopting and using new technologies. When we started with the MitraClip, we were one of five or six centres in Europe doing it'.

Giovanni Pedrazzini

But he says that not all devices are reimbursed. Hospitals must, therefore, decide whether they want to move ahead with using a new technology without a guarantee that they will be paid. 'One of the pending decisions is the reimbursement of TAVI, but it is a very complex application and it takes six months for a decision'.

However, Prof. Martin Cowie, an expert in both cardiology and health services research at Imperial College London, points out that it can sometimes be too easy to blame governments or other bodies for slow implementation when they must differentiate between what is true innovation and what is just new.

'In the case of the UK National Institute for Health and Clinical Excellence (NICE), there are very few developments in cardiovascular disease that they haven't supported. Sometimes it's a question of timing and the SHIFT study is a good example of where it can work well. Ivabradine was given a license for use in heart failure in February, and there is a health technology assessment being done and due to come out in the autumn – partly because the company had flagged it up early on'.

He says that companies and universities have an important part to play in providing the evidence. 'If you get that all lined up – if you come to market with two large trials and cost-effectiveness data, you stand a better chance. Look at dabigatran in the UK – it only took NICE two weeks from it being licensed to say OK'.

Martin R. Cowie

Prof. Cowie adds that those making decisions on health policy are getting quicker and in the UK both the previous and current governments have been keen to speed up the adoption of new technologies. He does, however, issue a note of caution: 'If it doesn't look like innovation, then it shouldn't be approved. We probably don't have an unreasonable balance between risk and innovation and we need to be aware that the public is not forgiving when risky things get through'.

Emma Wilkinson, MA freelance journalist

Setting minimum standards for interventional cardiology in France

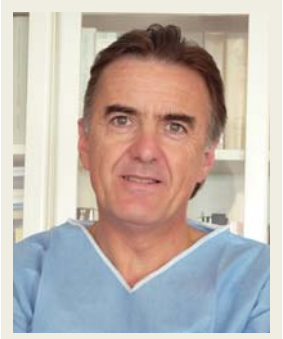
In 2009, the French government set out minimum standards for institutions that wish to carry out interventional cardiological procedures. Helen Jaques looks at why the rules were implemented and their effect

Back in 1998, France had an average of 2.7 angioplasty centres per million population: 210 centres that performed cardiac catheterization, 164 of which also performed therapeutic interventions.[1] However, there were considerable variations in the number of procedures performed at the interventional catheterization centres: three-quarters (75%) did >200 angioplasties per year, 48% >400 angioplasties per year, and 30% >600 angioplasties per year.

The rules

Given that the number of interventions a cardiology centre performs a year is known to have an inverse relationship with patient outcome,[2,3] the Groupe Athérome coronaire et Cardiologie Interventionnelle (GACI) of the Société Française de Cardiologie (French Society of Cardiology) decided to look into setting a minimum number of procedures interventional cardiology centres in France should perform.[1] Research from the USA suggests that a cut-off of 400 angioplasties a year would be a good threshold above which mortality and complication rates would be reduced,[4,5] and as such, guidelines in the USA recommend that percutaneous coronary intervention (PCI) should be done only at centres that perform >400 interventions year.[6]

In 2000, GACI recommended that cardiac institutions in France should do at least 400 therapeutic catheterizations a year, with 600 interventions a year being the optimal threshold. Subsequently, in April 2009 the French government passed legislation stating that every year interventional cardiology institutions must do a minimum of 50 acts of endocardial ablation other than the removal of the atrio-ventricular junction; 40 interventional catheterizations in children, including possible re-operation in adulthood of congenital heart disease; and 350 acts of coronary angioplasty.[7–9] The ruling also specified that the centre must also be open 24 h a day every day of the year.



Dr Paul Barragan

The threshold of 350 angioplasties a year set out in the government ruling is a 'compromise', says Dr Paul Barragan, who works at the Cardiovascular and Interventional Radiology Centre at Polyclinique les Fleurs in Ollioules. The French Society of Cardiology would ideally have had a higher number, but picking a value too high would force too many centres to close and affect access in some regions of France, he explains. 'I think it works because France has the lowest cardiac mortality (35 per 100 000 population) of the Organisation for Economic Co-operation and Development (OECD) countries and not only due to our red wine!' he adds. It's likely that these thresholds will increase in the future though once centres have had time to fully assess and reconfigure their services, says Prof. Eric Van Belle, who is in charge of interventional cardiology in the vascular cardiology and pulmonary division at Centre Hospitalier Régional Universitaire de Lille. 'At the end I think the idea would be to go to centres doing about 500 PCIs a year', he says.

Interestingly, the government ruling does not comment on the number of interventions an individual cardiologist should perform a year, despite GACI recommending that interventional cardiologists must do at least 250 diagnostic catheterizations a year in the first few years after finishing training and a minimum of 125 therapeutic catheterizations a year thereafter. However, France chose to introduce thresholds for institutions rather than for individual cardiologists to avoid discriminating against doctors who have a lot of research or education commitments and might struggle to reach a certain minimum, according to Dr Barragan.

The effects

In Paris, two small-to-medium-size cardiology centres have merged with Hôpital Pitié-Salpêtrière, one of Europe's largest hospitals, in the past few years to create the highest volume centre in the city. Paris actually had too many cardiology centres for its population, so the authorities helped to decide which centres should shut down or merge with another smaller centre or a big centre, says Prof. Gilles Montalescot, head of the cardiac intensive care unit in the Institute of Cardiology at Hôpital Pitié-Salpêtrière.

Prof. Gilles Montalescot

Patients who would have otherwise gone to these two centres do now need to travel a potentially further distance to get to Hôpital Pitié- Salpêtrière, he says, but given that all the centres were within the same city, the travel distances resulting from the merger are not too large. 'It could have a bigger impact in areas with a limited population where centres are small and patients will have to go further to get treated though', he adds. It's a similar story in the south of France, where five institutions have closed this year because they have not been doing a sufficient number of angioplasties, says Dr Barragan. 'But there are too many centres in the south of France', he adds. 'Instead of having two teams in two centres, the two teams will now be concentrated in one centre. That works well for everybody'.

It's not yet clear whether the mergers and the subsequent increase in volume in the interventional cardiology department at Pitié-Salpêtrière have improved patient outcomes at the centre. One reason is that a big volume centre with lots of different facilities tends to receive sicker patients, says Prof. Montalescot. 'Other hospitals and emergency services feel that it is very appropriate to send these patients to our institution, so smaller centres tend to get lower risk patients in the catheterisation lab and get on average, possibly, better outcomes', he says.

Nevertheless, the ruling will eventually prove to be beneficial to patients with heart disease in France, according to Prof. Van Belle. If a centre is open every hour of the day and provides the minimum number of interventions, patients can be guaranteed a minimum level of quality. There's also the fact that centres cannot be so far apart that the travel distance to one or the other would risk patients' lives, which guarantees revascularization services to all patients in the local population. 'I think the ruling is definitely a step in the right direction', he says.

Helen Jaques, freelance medical writer and editor

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