Cardiovascular imaging

An European Society of Cardiology/European Association of Cardiovascular Imaging task force is examining the appropriate use of cardiovascular imaging in Europe

Cardiovascular imaging (CVI) is evolving rapidly, placing new demands on our profession for training, education, and advocacy. It is likely that the need for CVI will continue to increase over the coming years due to the changes in cardiovascular disease epidemiology and ageing of the population. However, there are major inequalities in the access to CVI across Europe with important restrictions in some European regions reported recently. Furthermore, reliable statistics on the current CVI practice in Europe are lacking. Establishing the current status of the use of CVI in Europe has thus become an urgent priority.

Recent evidence indicates that a considerable percentage of medical imaging studies are unnecessary or inappropriate. The FDA estimates that 30–50% of all medical imaging exams are not medically necessary. Are these figures transferable to Europe? Intuitively, the explosive growth in CVI use could be similar in all industrialized countries.

Currently, there is growing interest in the scientific community in the appropriate use of CVI techniques for diagnosis and decision-making in Europe. Determining the appropriateness of individual medical imaging procedures is however challenging, since the relevance of CVI may vary with patients’ characteristics, local facilities, the degree of expertise of the imagers, and the rapid evolution of the imaging technologies.

The EACVI leadership at the behest of its current president, Prof. Patrizio Lancellotti, and with the help of Professors Gilbert Habib, Sven Plein, and Danilo Neglia, has decided to create a dedicated European Society of Cardiology/European Association of Cardiovascular Imaging (ESC/EACVI) Taskforce on CVI whose mission is to summarize and present the main issues pertaining to our knowledge of the appropriate use of CVI in Europe.

The major goals of the Taskforce are (i) to carry out surveys on CVI practice in Europe; (ii) to define appropriateness criteria and describe appropriate and inappropriate CVI use cases; (iii) to improve awareness of the appropriate use of CVI in Europe; (iv) to provide healthcare providers with information about the utilization of CVI in Europe; (v) to position ESC/EACVI as the referenced multi-modality CVI body towards European institutions; (vi) to become a federating body for exchange with other imaging specialists (in particular Radiologists and Nuclear Imaging Specialists); (vii) to carry out prospective registries and outcome studies on imaging.

Action plan as follows:

1. A mapping of the use of CVI techniques for diagnosis and decision-making across Europe represents the first comprehensive project of the ESC/EACVI Taskforce on CVI. Country-specific data will be gathered through different sources, in particular the National Societies. A ‘Cardiovascular Highlight book’ will contain data from a survey of the current use of CVI in the ESC membership countries. The project has been recently launched and 19 countries have already returned the required data.

2. Owing to the growing demand for diagnostic CVI, the development of criteria to aid appropriate use and planning of CVI availability becomes essential. Developing and implementing appropriateness criteria for CVI is thus another key objective of the Taskforce. By establishing appropriateness criteria, the ESC/EACVI Taskforce aims to safeguard the interest of the patients, of society as a whole, and of the ESC/EACVI community while promoting homogeneous healthcare provision, and implementation of guidelines and of evidence. Madalina Garbi, EACVI board member, has played a key role in the finalization of the first document focusing on the appropriateness criteria development process, which will soon be published in the EHJ-CVI. Future Taskforce appropriateness documents will focus on specific clinical conditions such as heart failure or ischaemic heart disease.

3. Although the value of imaging in the management of patients with cardiovascular disease is indisputable, the impact of imaging on clinical outcomes requires additional evidence. Therefore, the ESC/EACVI Taskforce will also set up prospective outcome studies, which aim (i) to strengthen the clinical value of CVI in the diagnostic work-up; (ii) to define the respective value of each imaging modality according to a specific clinical context; (iii) to determine how CVI may affect clinical decision-making and outcome. To reach these objectives, the ESC/EACVI Taskforce will use available data from large ESC registries or create new prospective registries on specific clinical conditions (i.e. heart failure, cardiac-oncology) or will implement new upcoming ESC registries with targeted imaging questions. With the help of the Committee for Research and Innovation of the EACVI, European projects will be drawn up to raise the required funds.
A case of translational research: calcium transport in cardiomyocytes suggests novel approaches to treating arrhythmias

Understanding electrophysiological events at the near-molecular level is pointing to new ways of treating arrhythmias: physician-scientist Prof. Karin Sipido, MD, PhD (Editor-in-Chief of *Cardiovascular Research*) is working to translate her findings to the clinic, reports Barry Shurlock PhD

One of the features of biomedical research over the last couple of decades is that the science has become so complex that there is a danger of clinicians and researchers running on parallel tracks that never meet. The so-called ‘translation gap’ between scientific research and clinical practice has, of course, received a lot of attention, but, like the ‘too much published’ problem, there are no easy answers. In principle, the growing presence of the physician-scientist has done much to bridge the gap, as clinical and bench research have become more specialized, and fewer and fewer physicians are to be found in basic research laboratories. Someone who is acutely aware of this is Prof. Karin Sipido, MD, PhD, who is head of experimental cardiology at the Catholic University of Leuven, Leuven, Belgium.

She said: ‘One of the points that I’m always bringing up in discussion is that it’s very important to maintain exchanges and interactions between clinically trained people and researchers, as there are now very few scientists with clinical training that go into full-time research. I go to the AHA and ESC meetings, as well as to the meetings of the Biophysical Society and Physiological Society. But, we are few to do so, a dying breed!’ Scientists with a PhD in life sciences and different specialty training are well positioned to lead the experimental research lab, while clinicians have the knowledge, expertise, and access to patients to provide the translation, forward and reverse. Partnership between these experts is the way to go’.
Prof. Sipido manages to combine an active academic career with involvement in a large number of bodies concerned with fostering research, locally, nationally, and internationally. Last year, for example, she became Editor-in-Chief of Cardiovascular Research and President of the Alliance for Biomedical Research in Europe, which represents 21 medical societies and 400,000 researchers in the EU.

She has been a board member of the ESC (2004–06) and was co-founder, and subsequently chair of the Council on Basic Cardiovascular Sciences. She is also a member of the EU affairs committee responsible for research and has been a member of the Basic Science Council of the AHA. Closer to home, she has chaired the Research Council of the Catholic University of Leuven and was Research Coordinator for Biomedical Sciences. In the Flanders region of Belgium, she is a Board member of the Center for Medical Innovation.

For people with such a strong administrative load, the laboratory bench is often a distant memory, but not for Prof. Sipido. She continues to publish ground-breaking research, working with a group of young enthusiastic postdoctoral and PhD students from all over the world. Dr Sipido’s main field of interest is cardiac cellular electrophysiology and calcium homoeostasis, especially the changes associated with cardiac hypertrophy and heart failure. In collaboration with other groups, she relates cellular data with in vivo findings. She is particularly interested in the role of altered calcium homoeostasis in cardiomyocytes, its role in arrhythmogenesis, and the potential for targeting NCX (sodium calcium exchange) as therapy. Recognition of her contributions has been marked by recent awards. In 2012 she was commended and accepted as member of the Academia Europaea, and last year she received the Keith Reimer Award of the International Society for Heart Research.

Much of her work is done with a fine ‘patch pipette’, only 2 μm in diameter, which is placed on the surface of isolated cardiomyocytes to record ion transport, while at the same time observing events within the cell by means of a fluorescent indicator for cytoplasmic calcium ion concentration and using confocal imaging. In this way, it is possible to understand events in subcompartments and microdomains of the cell, extending, with the latest techniques, down to the level of clusters of a few molecules. Importantly, this work shows how calcium transport is altered in cardiomyocytes from people who have suffered a myocardial infarction.

Beyond the sheer elegance of these techniques, Prof. Sipido is confident that the findings contribute to identifying novel kinds of antiarrhythmic therapy. She said: ‘We have shown that NCX is closely involved in the generation of arrhythmias. Despite advances in the use of implantable cardioverter-defibrillators, there is a definite need for new drugs – a very different kind of drug from classic drugs. NCX provides a new target for drug therapy, so that by mild suppression of this kind of calcium transport, combined with other targets, we believe it will be possible to improve the treatment of arrhythmias’.

One of the reasons why Prof. Sipido and her colleagues are able to carry out such sophisticated studies is that the Department of Cardiovascular Sciences and the University Hospital in Leuven provides an excellent research environment. The Department has 60 faculty members, with a wide range of expertise, including molecular biology, in vivo imaging, cell models, patient studies, and large clinical trials. Importantly, the Division of Cardiac Surgery performs 20–25 heart transplants a year, and there is a dedicated, round-the-clock, on-call team of scientists able to work on explanted hearts. Additional work is done on small heart biopsies obtained during valve surgery. She said: ‘There are very few studies of human cardiomyocytes, which are difficult to obtain. The problem is that the tissue samples are either very small or from very diseased hearts and it’s therefore very difficult to isolate single working cells. It doesn’t lend itself to the sort of protocols used in animal studies with pigs and sheep. The department also has initiated several clinical proof-of-concept studies, and this potential for translation, within one department, creates a very attractive and powerful research environment’.

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**GAP-AF study helps to define optimal approach for atrial fibrillation ablation**

**Result of late breaking trial presented at European Heart Rhythm Association EUROPACE 2013**

Using catheter ablation to create complete linear lesions around pulmonary veins proved more effective than the creation of incomplete lesions in preventing recurrence of atrial fibrillation (AF), reported the GAP-AF study. The study, presented in the Late Breaking Clinical Trials session I at the EHRA EUROPACE 2013 meeting in Athens, Greece, represents the first time that a randomized controlled study has been undertaken comparing the two different ablation strategies for patients with paroxysmal AF.

Identification of triggers initiating AF within the pulmonary veins led to prevention of AF recurrence by catheter ablation at the site of origin of the trigger. The Heart Rhythm Society/European Heart Rhythm Association/European Society of Cardiology Expert Consensus Document on Catheter and Surgical Ablation of Atrial Fibrillation (published in 2007 and updated in 2012) states that patients undergoing catheter ablation for AF should have complete isolation of the pulmonary veins, which involves a complete circumferential lesion being created around the pulmonary vein.
‘This recommendation was based on observational studies, not on a prospective randomized trial. But some electrophysiologists (EPs) continue to believe that it’s sufficient to create incomplete linear lesions where conduction sites still exist between the pulmonary veins and left atrium’, explained Prof. Karl Kuck, from Asklepios Klinik St George, Hamburg, Germany, presenter of the GAP-AF study.

Part of their reasoning is that 95% of patients with AF recurrence after complete pulmonary vein isolation (PVI) procedures are found to have conduction gaps between the pulmonary veins and the left atrium, he said. ‘Since they can’t isolate the pulmonary veins permanently, they reason that incomplete isolation is sufficient and has the advantage of being a shorter procedure with a potentially lower complication rate and less cost’, said Prof. Kuck.

In the GAP-AF (AFNET1) study between February 2006 and August 2010, 233 patients with drug refractory paroxysmal AF were randomized to have either a complete procedure (n = 117) or an incomplete procedure (n = 116). For the incomplete procedure, the EPs stopped the radiofrequency application at one site to permit reconnection from the circumference. The study, which was performed in seven German centres, was funded by the German Atrial Fibrillation Network (AFNET). The inclusion criteria for the study were that patients had to be aged over 55 years and to have been treated with one antiarrhythmic drug before they entered the trial. Patients with poor left ventricular function were excluded from the study.

The primary endpoint of the study was the time to first recurrence of symptomatic AF with duration of ≥ 30 s on trans-telephonic ECG monitoring, or detection of asymptomatic AF defined as two consecutive recordings of AF during a minimum of 72 h. The study made use of the RhythmCard™ technology, a small credit card-sized device that patients can place on their chest wall to record an ECG whenever they experienced symptoms of AF and transmit the data via the telephone. Additionally, patients were asked to record and transmit an ECG every day regardless of their symptoms.

Results showed that at the 3-month follow-up, sinus rhythm had been achieved in 37.8% (46) of patients who had complete ablation, vs. 20.8% (26) with incomplete ablation (P < 0.001).

At 3 months, when patients were taken back to the EP lab for a repeat investigation, 70% of those randomized to complete PVI had gaps vs. 89% randomized to incomplete PVI.

No significant differences were found for serious adverse events (including syncope, stroke, major bleeding, and tamponade) between the complete and incomplete groups.

‘The study shows us for the first time that complete isolation of the pulmonary veins is more effective than incomplete isolation. It suggests that the level of evidence for complete ablation should be upgraded from class Ic to class Ia, where it is supported by a multicentre randomized trial’, said Prof. Kuck.

However, the study also highlighted that recurrence rates were high even for patients who had undergone complete isolation procedures. ‘Research is urgently needed to improve ablation techniques to make the complete lines more durable. There is a need to explore other energy sources and tools for catheter ablation’, he said.

The fire and ice trial, for example, is currently underway to see whether a thermoCool catheter might be more effective than cryoablation for patients with paroxysmal AF.

Study of Ablation versus AntiArrhythmic Drugs in Persistent Atrial Fibrillation study shows ablation superior to drugs for patients with persistent atrial fibrillation

Results of late breaking trial presented at European Heart Rhythm Association EUROPEACE 2013

The Study of Ablation versus Antiarrhythmic Drugs in Persistent Atrial Fibrillation (SARA) study, presented in the Late Breaking Clinical Trials session at EHRA EUROPEACE 2013, found that catheter ablation (CA) therapy was superior to medical therapy for maintenance of sinus rhythm in patients with persistent AF.

While a number of previous studies have shown the superiority of CA over anti-arrhythmic drug therapy (ADT) for patients with...
paroxysmal AF, no previous studies have been undertaken specifically comparing ablation to drugs in patients with persistent AF.

Principal investigator Prof. Lluis Mont, from the Atrial Fibrillation Unit, University of Barcelona, Spain explained, ‘Patients with persistent AF have in general been considered bad candidates for ablation due to poor results and the need for prolonged and aggressive procedures’.

Between May 2009 and November 2011 in the open parallel SARA study Prof. Mont and colleagues, from eight ablation centres in Spain, randomly assigned a total of 146 patients with persistent AF 2:1 to CA (n = 98) or ADT (n = 48). Antiarrhythmic drug therapy was given according to current guidelines, with class III drugs (amiodarone) recommended for patients with structural heart disease and class Ic (flecainide) plus diltiazem or beta-blockers for patients without structural heart disease. The inclusion criteria were: patients with persistent atrial fibrillation of >7 days, or <7 days that needed pharmacological or electrical cardioversion.

The study specifically excluded patients with chronic persistent AF (continuous for >1 year) since this represents a ‘bad scenario for ablation’ and also patients with extremely dilated atriums (>50 mm antero-posterior diameters).

In an intention-to-treat analysis, the proportion of patients free of prolonged (>12 h) AF at 12 months (primary endpoint) was 70.4% in the CA group vs. 43.7% in the ADT group (P = 0.002); implying an absolute risk difference of 26.6% (95% CI: 10.0–43.3) favouring the ablation group.

The proportion of patients free of any recurrence of AF or atrial flutter (lasting >30 s) was 60.2% in the CA group compared with 29.2% in the ADT group (P < 0.001).

The take-home message is that AF ablation in persistent AF has a reasonable success safety profile and can be offered to patients resistant to ADT, provided some specific selection criteria are applied, such as excluding patients with very dilated atrium and longstanding persistent AF”, said Mont.

One weakness was that the study only recruited patients from arrhythmia units. ‘Therefore they’re likely to represent a selected population resistant to ADT’.

A challenge for increasing the number of ablation procedures taking place was likely to be the shortage of highly trained physicians. ‘But as happened years ago with coronary angioplasty, the demand is likely to increase the numbers of physicians and centres prepared to perform such procedures’, said Prof. Mont.

Further studies, he added, are now needed, to look at outcomes according to ‘shape remodelling’ and levels of fibrosis. ‘This should help to further stratify patients and select good candidates for ablation’, he concluded.

Andros Tofield

Catheter ablation of atrial fibrillation as first-line treatment: is the future here now?

The prevalence of atrial fibrillation (AF) in Europe is increasing.1 Despite the benefits of maintaining sinus rhythm,2 pharmacological strategies have not provided satisfactory results in randomized studies, probably because their beneficial antiarrhythmic effects have been offset by their adverse effects, and even increased morbidity and mortality have been observed. Since the initial work done by Haissaguerre et al.,3 catheter ablation of AF has undergone remarkable evolution. It has become a more standardized procedure, with better results and lower complication rates. The key to offering catheter ablation to an increasing number of patients is to find a way of combining good clinical results with very low complication rates.

During the last decade multiple randomized trials have been published, comparing catheter ablation treatment to antiarrhythmic therapy. Most of these studies have been conducted in patients with paroxysmal AF refractory to one or more antiarrhythmic drugs. They have shown that ablation is more effective than antiarrhythmic therapy in preventing recurrences, with follow-up periods from 9 to 12 months. Although the evidence is less, we do have data from randomized trials that also show greater efficacy in patients with persistent AF refractory to antiarrhythmic therapy. The SARA study is the first multicentre, randomized study to compare antiarrhythmic therapy to catheter ablation in patients with persistent AF of <1 year. After a 12-month follow-up period, significantly fewer patients in the ablation group had a recurrence of AF or atrial flutter lasting >24 h, or need for cardioversion.4

New evidence of the usefulness of ablation has been added with the publication of trials studying ablation as first-line treatment for patients with paroxysmal AF.5,6 In 2012 Cosedis et al. published a multicentre, randomized study comparing AF ablation as first-line therapy to antiarrhythmic therapy in 294 patients with a history of paroxysmal AF who were followed for 2 years. At the end of follow-up, the probability of remaining free of AF (85 vs. 71%, P = 0.004) and symptomatic AF (93 vs. 84%, P = 0.01) and the quality of life, were significantly higher in the ablation group. However, the cumulative burden of AF was not significantly different between the two treatment groups (13 vs. 19%, P = 0.1).7 In the RAAFT 2 study, a significant decrease in time to first AF was observed in patients treated with ablation as first-line therapy (54 vs. 72%, P = 0.01).5 Because of these study results, the indication for catheter ablation as first-line therapy in patients with paroxysmal AF was raised in the 2012 focused update of the European guidelines for AF treatment to IIa (level of evidence B)8 from the previous guideline’s IIb (level of evidence B),8 thus supporting the idea that AF ablation has already crossed the tipping point and become first-line therapy. The guidelines state that AF ablation as first-line treatment should be...
considered in selected patients with symptomatic paroxysmal AF, provided that the procedure is performed at experienced centres and account is taken of the preferences of patients, who must be adequately informed about the efficacy and safety of the different treatment options available. In addition to guidelines, clinical characteristics can help in the selection of patients for whom AF ablation is an option. In cases with frequent paroxysms of AF, we can offer higher success rates with a procedure for the ablation of atrial ectopic foci that display frequent activity, in addition to electrical isolation of the pulmonary veins, especially if the foci are shown to trigger AF (Figure 1).

The same happens when paroxysmal supraventricular tachycardia is suspected to cause AF. We also believe the patient must be motivated and willing to undergo repeat ablation procedures, because data have shown a high recurrence rate in the medium term (4–5 years) after ablation and we know repeat ablation improves efficacy. Recent research has been providing encouraging results regarding the identification of areas involved in AF maintenance in individual cases, opening the door to more-targeted ablation strategies. Furthermore, the development of ablation techniques and the growing experience of professionals performing ablation are enabling us to treat our patients with increasingly safe and more effective procedures. That is why AF ablation as first-line therapy is already here.

We believe that the future development of the technique will eventually broaden the indications to even include selected patients with asymptomatic AF episodes, as happened in the past with the ablation of other arrhythmic substrates, such as typical atrial flutter and accessory pathways.

**References**


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