Imaging

Invasive coronary imaging: any role in primary and secondary prevention?

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This review discusses the possibilities offered by new modalities of non-invasive and invasive coronary imaging in an effort to optimize risk stratification for coronary artery disease, and identify subgroups at high risk that may benefit from an aggressive, personalized approach, with access to a growing number of novel drugs and interventions. Special emphasis is placed on the progress of novel invasive imaging techniques such as near infrared spectroscopy and optical coherence tomography that can reliably identify thin-capped fibroatheromas. Multiple trials are exploring the feasibility of these techniques to guide modulation of risk factor control and treatment of non-flow limiting lesions at high risk of destabilization and progression in patients undergoing clinically mandated angioplasty of angiographically critical lesions. Asymptomatic patients at high risk of cardiovascular ischaemic events may also benefit, with the intermediate step of a wider application of calcium score and angiography with multi-slice computed tomography, by a selective use of invasive imaging.

Keywords

Intravascular ultrasound • Near infrared spectroscopy • Optical coherence tomography • Coronary multi-slice computed tomography • Coronary atherosclerosis

Introduction

Interventional cardiologists playing surgeon in their scrubs, and prevention specialists never wearing a white coat appear to be the two extremes of cardiology, the busy ‘doer’ treating acute coronary syndromes, and the ‘thinker’ lobbying against the tobacco and fast food industry. They are often perceived as competitors for the shrinking pot of health budgets, arguing on the relative merit in the sustained decrease of cardiovascular mortality in the last decades, a merit they probably share almost equally, and the cost effectiveness of complex angioplasty vs. population-based interventions. This article supports the concept that they should work more together. New developments in interventional cardiology and intravascular imaging offer the opportunity to help in the triage of patients with a previous cardiac event but also of ‘healthy’ individuals with high cardiovascular mortality at 5–10 years despite intense medical treatment.

Unmet needs: secondary prevention

Morbidity and mortality remains high in patients with overt symptoms caused by coronary atherosclerosis, especially after acute

coronary syndromes. Most importantly, more than half of the late events developing after coronary angioplasty do not involve the stented segment.¹ Considering the success of second-generation drug-eluting stents in reducing thrombosis and restenosis, the relative importance of disease developing in non-culprit arteries and segments can only increase. The problem does not lie in additional critical lesions that can be treated at the time of primary angioplasty or soon after, but in the segments with severe atheromatous burden which appear as non-critical lesions or small irregularities or totally normal with angiography and remain untreated. Bypassing most of the segments at risk of disease progression makes multi-vessel bypass implantation more effective in the protection of patients with diffuse complex atherosclerosis, especially if diabetic.² Focusing treatment to flow limiting lesions may not prevent events caused by disease progression, but at the same time, grafting or stenting all arteries with minor irregularities is not a solution. Grafts to arteries without critical stenoses have lower patency rate due to competition of flow. We need techniques guiding us to the identification of patients and lesions at high risk of progression and destabilization. In symptomatic patients undergoing angioplasty to treat the culprit lesion, we have the luxury of having already access to the coronary tree with catheters and guidewires. Fractional flow reserve (FFR) in non-culprit arteries with intermediate stenoses has been

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proposed at the time of acute treatment in STEMI patients and is widely adopted in NSTEMI patients. Intracoronary intravascular ultrasound (IVUS) is frequently used for optimization of the angioplasty results and optical coherence tomography (OCT) and near infrared spectroscopy (NIRS) have been shown to offer specific advantages in the treatment of thrombus containing lesions and in the identification of the culprit lesion, predicting the chances of embolization. The same catheter already utilized for the assessment of the culprit vessel can be used for a quick study of the other coronary vessels and segments, at no additional cost. Of course you may say that all patients with a previous ischaemic event should engage anyway into the strictest prevention programs, so that a further triage does not change the treatment strategy. We all know, however, that the reality is different, and only a minority of patients remain compliant with the strict lifestyle changes required. Most patients quickly lose the initial motivation to regularly use the multiple medications needed to control their risk factors. If we manage to concentrate our efforts in the group at higher risk, we may increase their compliance with regular follow-up visits, and anticipate new acute events with frequent provocative tests. The comparison between patients left with usual care, often with no more than a yearly visit to a GP to renew prescriptions, and patients in trials, regularly seen by specialists and research nurses boosting their motivation, have shown that compliance to statins can increase from 30–40% to >80%, both in primary and secondary prevention.³ Furthermore, since adverse events occur despite full implementation of the available preventive measures and treatment, intravascular imaging may help us to explore new treatments, targeting this high-risk group in clinical trials and giving priority access to them in the initial phases of clinical application.

A gigantic unmet need: primary prevention

Current conventional, clinical approach to a patient entering our office for a ‘cardiac check-up’ will be to input age, weight, sex, family history, smoking habits, cholesterol level, presence of hypertension, or diabetes into a calculator providing the 10-year risk of events based on large longitudinal studies⁴ (Table 1). A method to risk-stratify patients and concentrate the effort on high-risk cohorts is appealing, and may be cost-effective. However, this approach does not suit the clinician who meets an individual patient, with

his fears and symptoms, and may not feel satisfied by a generic standardized advice. The question is whether he or she has clinically significant coronary artery disease, or is developing it, and how hard he/she needs to fight to prevent progression. We all have the experience of catastrophic myocardial infarctions in the odd young female with poor family history and hypercholesterolaemia, who did not fulfil criteria to perform further investigations or start preventive measures (Figure 1). At the other end of the spectrum, in patients with double-digit risk at 10 years, the risk reduction you can offer with conventional prevention approaches is far from satisfactory. Neglecting the different individual needs may bear negative clinical consequences for the patient, and legal risks for the doctor. Invasive imaging in an asymptomatic patient sounds like blasphemy. However, the selection of the few candidates who may benefit from this approach is facilitated by the significant progress in non-invasive coronary imaging. Coronary multi-slice computed tomography (MSCT) has the obvious advantage to detect coronary atherosclerosis at early stages before ischaemia develops, and becomes detectable in provocative tests. With technical development reducing the radiation burden, you may argue that MSCT angiography can be offered more liberally in middle-aged or older individuals. A totally negative MSCT coronary angiogram with no calcium and pristine arteries is obviously very reassuring. In patients truly intolerant to statins, we may relax our firm prescriptions and opt for less onerous lifestyle changes. Other patients will show significant atheromatous burden but absence of critical stenoses, allowing reassurance on the absence of immediate threats, but offering a strong argument to force the patient to engage in an intense prophylaxis. Some patients will show >50% coronary lesions that may require coronary angiography, ending up with stenting functionally significant lesions. These patients will automatically move from primary to secondary prevention and qualify for invasive imaging techniques able to identify non-obstructive, high-risk plaques, responsible for future coronary events (Figure 2).

Progress in intravascular imaging

Intravascular ultrasound: IVUS is an established technique with >25 years of application in cardiovascular medicine (Table 2). Like for other intravascular imaging techniques using sub-millimetric flexible catheters, the risk of adverse events such as spasm, dissection, and thrombosis is extremely low provided active premedication is used

Table 1 Estimates of cardiovascular disease risk for hypothetical patients derived from the HeartScore calculator (<https://escol.escardio.org/HeartScore/calcResult.aspx>)

Age, sex, cholesterol (total/HDL in mmol/L), systolic blood pressure, smoking habit	HeartScore CVD level (%)	10-year cardiovascular risk
65 y.o. male, TC 6.5, HDL 0.8, 160 mmHg, light smoker	16	Very high: >15%
66 y.o. male, TC 5.8, HDL 1.1, 174 mmHg, never smoked	9	High: 2.0–15%
60 y.o. male, TC 4.7, HDL 1.3, 138 mmHg, never smoked	2	Intermediate: 0.5–2.0%
47 y.o. female, TC >8, HDL 1.3, 140 mmHg, heavy smoker	0	Low <0.5%

HDL, high-density lipoprotein cholesterol; TC, total cholesterol.

Figure 1 A 39-year-old woman with long lipid-rich plaque shown with NIRS-IVUS undergoing primary percutaneous coronary intervention because of anterior STEMI. Despite a transient low-flow phase after balloon dilatation an excellent result is achieved with two long stents. Images from 1 to 4 correspond to the culprit lesion (arrows in the angiographic panel) immediately after implantation of a 3.5 mm second-generation drug-eluting stent. In 3–4, the presence of lipid rich plaque at the likely site of rupture, occupying two vessel quadrants, is clearly indicated in the circumferential ring around the intravascular ultrasound images. A higher lipid content burden index (605) is present in the most heavily infiltrated 4 mm of a separate second plaque more distal to the original site of occlusion. If this normotensive lady was seen the day before the event, a smoker with family history of coronary artery disease, a total cholesterol of 7.6 and low-density lipoprotein 4.76 mmol/L and heavy smoker, her cardiovascular disease risk at 10 years was calculated as equal to 0.

with heparin and nitrates. Intravascular ultrasound allows for diagnosing large plaque burden, which is associated with poor clinical outcome. Multiple studies have confirmed that the percent cross-sectional area occupied by plaque is the most powerful predictor of events.^{1,5,6} Large regression studies have shown that intense pharmacological treatment with statins can slow down or halt progression and possibly promote partial regression, while conventional recommended doses are still associated with an increase in plaque volume over time.^{7,8} Since IVUS has limitations in the identification of plaque components, radiofrequency analysis has been advocated as a possible solution. The currently available algorithms, so-called virtual histology (VH), are in fact based on pattern recognition and provided controversial results in validation studies.⁹ When used in a regression study with high-intensity rosuvastatin in 103 STEMI patients, the reduction in total plaque volume was not mirrored, as expected, by a reduction of lipid component.¹⁰ Thin-capped fibroatheromas (TCFAs) are identified by the lack of separation between a large pool of red-encoded necrotic core and the lumen assuming that if IVUS cannot visualize the intimal cap this is below its axial resolution of 100 μm . This limitation may explain why TCFA assessed by VH has low predictive value of events in itself, and only offers some additional value when combined with plaque burden and a small lumen cross-sectional area.^{1,6}

High-frequency IVUS with a large bandwidth has been advocated to improve resolution maintaining the ability to image through blood. Resolution is an inherent limitation of a technique based on the relatively low frequency of ultrasound and the undeniable quality improvement offered by recently introduced new IVUS systems does not eliminate the need to switch to light as a real game changer. Two new techniques have the potential to overcome the limitations of IVUS, NIRS, offering a quantitative chemogram of the vessel wall with clear recognition of lipids,¹¹ and OCT, an imaging technique with a resolution of 10 μm providing exquisite details of the superficial plaque components including the fibrous cap.¹²

Optical coherence tomography: OCT works in a wavelength range absorbed by haemoglobin and requires blood removal, a limitation in part overcome by the very rapid acquisition. With the present systems generating 160–180 lines/s, a sufficient density per cross-section is maintained at very fast speed (up to 2–3 cm/s), allowing image acquisition in few seconds along several centimetre of artery (up to 10 cm), while the blood is displaced by contrast or dextran. The second problem of OCT is penetration that can be as low as 0.5 mm in plaques with high attenuation containing lipids. Therefore, OCT is unable to generate a circumferential image of the artery including the adventitia in most plaques, except segments with very thin intimal hyperplasia. As such, OCT cannot estimate plaque

Figure 2 A 44-year-old woman undergoing multi-slice computed tomography non-invasive coronary angiography because of partially atypical chest pain. The severe serial lesions in the left anterior descending artery detected with computed tomography are confirmed with invasive angiography and optical coherence tomography, showing a very severe circumferential thin capped fibroatheroma (lesion site, A). Despite multiple risk factors including smoking and severe hypercholesterolaemia, the 10-year cardiovascular risk was 0 based on conventional parameters.

Table 2 Technical characteristics, advantages, disadvantages, and unique added value of the various intravascular imaging techniques for detection of vulnerable plaques

Imaging technique	Technical background	Advantages	Disadvantages	Unique added value
IVUS	Mechanical or electronic ultrasound-based imaging	Cross-sectional image of the entire vessel wall including EEM	Poor resolution (100 μm) Shadowing behind calcium Poor specificity in differentiating soft components (lipids, thrombus, and hyperplasia)	Vessel remodelling
VH	Detection algorithms derived from comparison with histology	Simple post-processing of conventional IVUS images, already implemented in most vendors' software	Sensitivity and specificity questioned by independent comparisons with histology, OCT, and NIRS	Only plaque composition method with long-term data on outcome (PROSPECT and VIVA)
OCT	Laser-generated near infrared light-based images	High resolution (10 micron) Rapid acquisition (frequency domain, 2–3 cm/s)	Limited penetration (requires flushing during acquisition, unable to show full plaque thickness)	Measurement of fibrous cap thickness
NIRS	Analysis of reflected spectrum of near infrared light	Reliable chemogram of the wall lipid content	Indicates circumferential distribution but not depth (but limitation partially overcome by simultaneous IVUS imaging with a single catheter)	Semi-quantitative assessment of wall lipids

EEM, external elastic membrane; IVUS, intravascular ultrasound imaging; OCT, optical coherence tomography; NIRS, near infrared spectroscopy; OCT, optical coherence tomography; PROSPECT, Providing Regional Observations to Study Predictors of Events in the Coronary Tree; VIVA, VH-IVUS in vulnerable atherosclerosis.

burden or remodelling. In acute coronary syndromes, OCT identifies plaque rupture and thrombosis in most cases. The absence of plaque rupture underneath thrombotic lesions suggests plaque erosion, the recognized mechanism of 15–20% of fatal thrombotic lesions in pathology studies.¹³ Rupture and thrombosis may be prompted by superficial protruding calcium nodules.¹⁴

Optical coherence tomography is the gold standard in the detection of TCFA, defined as lipid-rich plaques (LRPs) separated from

the lumen by a thin fibrous cap of <70 μm, and possibly infiltrated by highly reflective lines and dots representing macrophages. The OCT characterization of plaque components does not easily lend itself to methods of automatic quantification.

Near infrared spectroscopy: The wavelength used in NIRS has minimal absorption by the red blood cells, avoiding the need for flushing, and has excellent penetration. However, NIRS lacks the ability to differentiate the depth of the various wall components. Typically,

NIRS signals are displayed as a circumferential band where lipids, with a maximal absorption at λ 1420 μm , are encoded in yellow, which is easily distinguished from the other wall components, displayed in red. The lipid content burden index (LCBI) is reported along the entire acquisition segment, or within the 4 mm segment of highest accumulation (LCBI_{4 mm}). Of clinical relevance, commercially available systems allow the simultaneous acquisition of IVUS and NIRS signals, potentially offering the opportunity of collecting information on lipid content in patients already studied for approved indications of IVUS such as optimization of stent expansion. This allows the simultaneous assessment of lipid content, lumen stenosis severity, and plaque burden.¹⁵ Studies in patients with STEMI and NSTEMI have shown that LRPs are reliably identified in the majority of patients, with a progressive increase in lipid content, moving from stable plaques to non-culprit arteries in ACS, and finally to culprit lesions in NSTEMI and STEMI patients.¹⁶ Furthermore, embolization after percutaneous coronary intervention (PCI) is correlated with high lipid content.¹⁷ In addition, the method of lipid identification is sufficiently robust to detect significant differences between the effect of high doses of rosuvastatin administered for few months and conventional statin treatment.¹⁸ Presence of LRP appears to have an additional, independent predictive value compared with classical risk factors. In a study of the relationship between LCBI in a non-culprit segment and clinical characteristics, blood lipids and hs-CRP, it was found that only 23.2% of LCBI variability was linked to the conventional determinants of a high cardiovascular risk profile and blood markers were of limited importance.¹⁹ A prospective observational study assessing stable and acute patients, found that the 1 year cumulative incidence of all causes of mortality, non-fatal ACS, stroke, and unplanned coronary revascularization was significantly higher in patients with an LCBI_{4 mm} equal to or above the median value (43.0) compared with those with an LCBI value below the median.

The recently started LRP study (NCT02033694) has completed enrolment of 1000 patients presenting for coronary angiography with clinical indications to IVUS of the culprit lesion. Results obtained by an IVUS-NIRS evaluation of non-culprit vessels and segments, will be related to major adverse cardiac events at 3 years. Another important ongoing NIRS study is the Chemometric Observation of Lipid Rich Plaque of Interest in Native Coronary Arteries (COLOR-NCT00831116) registry, which will identify the associations of LCBI with angiographic or clinical presentations of coronary artery disease. The IBIS-3 study results have been recently presented at PCR, showing no effect of high-dose rosuvastatin in promoting regression of the necrotic core assessed with NIRS.²⁰

Fusion imaging, already a reality for IVUS-NIRS, has the potential to increase accuracy in the prediction of high-risk plaque via the complementary information provided by these three imaging modality, able to detect the coexistence of lipid rich, positive remodelled plaques with large plaque burden, reduced lumen area, and thin fibrous cap.

From patient triage to individualized treatment

The current treatment of patients presenting with unheralded AMI/SCD is based on emergent catheterization and coronary stenting.²¹ Unfortunately, treatment is delivered when myocyte death already

induced permanent damage. The challenge is how to detect and treat the same lesions before rupture and thrombosis and a forward looking editorial of Braunwald already defined a role for imaging in asymptomatic individuals at high risk.^{22,23} The availability of non-invasive coronary CT angiography with very low radiation exposure during a single diastolic acquisition and calcium score adds a new dimension to the identification of very high-risk groups (Figure 3). Patients with CACS >1000 have 25% events per year. Patients with positive remodelling, spotty calcifications, and low attenuation with CT²⁴ have 22% risk at 2 years. Conversely, a negative result will re-classify these patients to a low-risk category. Extremely intense statin regimens are not needed to prevent disease progression if there are no atherosclerotic lesions to begin with, and statin-related side effects and repeated follow-up visits can be safely avoided allowing us to concentrate on truly high-risk individuals.

The main problem of coronary MSCT is the possibility of overestimating lesion severity, especially when prominent blooming artefacts due to calcification obscure the lumen. Overutilization of selective coronary angiography in questionable cases should be avoided with liberal use of non-invasive provocative tests. In some of these patients, however, results will remain positive or ambiguous and selective coronary angiography possibly followed by an FFR/imaging evaluation is indicated. Second-generation drug-eluting stents are safer and more effective than ever before, with stent thrombosis in stable lesions of <0.5% at 1 year, and nearly complete absence of late thrombosis due to highly biocompatible permanent polymers or biodegradable polymers. New stents offer the promise of slow drug elution and effective restenosis prevention in the absence of polymers or from small abluminal dots or wells of biodegradable polymers. Fully bioabsorbable stents are an even more appealing alternative. They are currently under investigation in the PROSPECT 2 ABSORB trial (clinicaltrials NCT02171065), with the aim to seal and promote fibrotic transformation of LRPs at risk, identified with an NIRS examination, with restoration of normal vasoreactivity and flow dynamics²⁵ and total elimination of the potential long-term risk and inconvenience of the persistence of a rigid metallic foreign body jailing branches and precluding bypass surgery. Still, data from real world registries in complex lesions showed a worrisome incidence of scaffold thrombosis (2.1% at 6 months), certainly worse than the expected natural history. High frequency of unstable and thrombus containing lesions, poor technique with rare post-dilatation, and IVUS/OCT assessment of scaffold apposition/expansion probably explained this high frequency of complications, potentially correctable with better technique.²⁶

After PRAMI,²⁷ CvLPRIT,²⁸ and DANAMI3-PRIMULTI,²⁹ it is generally accepted that treating bystander critical stenoses in STEMI patients reduces adverse events such as death, myocardial infarction, and urgent revascularization. FFR is already included in the recently reported DANAMI3-PRIMULTI study and a negative FFR excluded almost one-third of angiographically critical lesions. The opposite is also true. FFR not rarely turns out to be unexpectedly positive in long but angiographically moderate LAD lesions and, in stable patients with FFR-positive lesions, there is confirmation that PCI reduces the combined endpoint of death and myocardial infarction at 2 years.³⁰ Modern interventional cardiology has already established that we have to go beyond angiography to determine which lesions require a mechanical treatment.

Figure 3 Triage of the synergies between invasive and non-invasive imaging techniques available in high-volume centres.

Is there evidence supporting treatment in lesions not yet functionally significant but with morphological features of high risk? In patients with double-digit risk of events it looks logical but the previous longitudinal studies had too many limitations in the imaging techniques used, sample population size, duration of follow-up to provide a final answer. Precise measurement of cap thickness and reliable identification of lipid content with OCT and NIRS have the potential to overcome these shortcomings and develop sufficiently stringent criteria to identify the potential of progression of non-critical plaques. If we have two ACS patients with similar clinical risk profile but one with minimal disease outside the treated culprit lesion, the other with diffuse disease and multiple vulnerable plaques it is not rational to offer both the same standardized treatment. A much more aggressive series of preventive measures must be applied in the latter patient. We do not believe that focal mechanical treatment of all vulnerable lesions will ever become the cornerstone of prevention but it is legitimate to consider implantation of dedicated self-expanding or biodegradable stents in selected patients with focal high-risk lesions. There is an important conceptual caveat to this strategy. Atherosclerosis is a systemic disease causing multiple diffuse changes. In most patients, there are enough low or intermediate risk plaques to make it likely that, in the long run, if

lesion progression continues, most events will be caused by them rather than by fewer high-risk lesions. This concept is at the basis of the endless debate between supporters of the vulnerable plaque or vulnerable patient hypotheses. Even if you demonstrate that you can detect and treat with low complications high-risk lesions eliminating their rupture and destabilization, you should still continue focusing on the systemic treatment of the patient's risk factors to prevent events from low-risk plaques or newly developed plaques.

Intravascular imaging can measure the disease burden and allow an individualized response that goes beyond mechanical treatment of focal high-risk lesions. High-dose statins promote stabilization and regression of high-risk plaques and a big advantage can be obtained just promoting compliance with frequent controls, the cause for the better outcome of study patients also in the placebo arm.³¹ The benefit of apolipoprotein A-I Milan has been convincingly demonstrated in animal experiments³² and confirmed by reduction in plaque volume assessed with IVUS. The small trials performed did not show reduction of events^{33,34} and this promising treatment was prematurely abandoned because found to be too costly and too inconvenient for the patient, requiring repeated i.v. infusions, to be adopted in prevention therapy. A recent randomized trial with a different HDL-mimetic agent failed to show significant differences in

plaque volume but was not powered, like the previous trials, for event reduction and changes of plaque characteristics.^{35,36} Low-density lipoprotein plasmapheresis is another example of highly effective lipid-lowering treatment almost exclusively applied in a niche population of young patients with severe familial hypercholesterolaemia. Bariatric surgery is advocated to complement pharmacological treatment in patients with diabetes and expanded indications paralleled the advances in the technique and reduction of invasiveness. New pharmacological lipid-lowering agents are in the pipeline. Some, like mipomersen and lomitapide, may cause injection-site reaction, abdominal symptoms, and hepatic damage, prompting a careful selection of the candidates who will unequivocally benefit. Others, such as the monoclonal antibodies targeting proprotein convertase subtilisin kexin type 9 (PCSK9), seem to combine great efficacy and low risk of side effects but have the inconvenience of daily injections. Non-invasive screening of calcium score, MSCT coronary angiography and, in selected cases, invasive intravascular imaging can help to identify a threshold justifying the additional cost and discomfort of these novel treatments.

Conclusion and call to action

Cardiologists have developed a fatalistic approach toward high-risk coronary atherosclerosis. While every effort is made to gain minutes in opening occluded arteries with primary angioplasty during acute myocardial infarction, the paradigm for asymptomatic patients irrespective of their event risk is always conservative: *noli me tangere*, do not touch me. We currently recommend diet, exercise, smoking cessation, diabetic control, and statin therapy according to the guidelines. Even after an acute coronary event, a near miss or a full-fledged prolonged ischaemia with major myocardial damage, the strategy for secondary prevention is the same, just adding dual anti-platelet therapy. However, in a parallel comparison, oncologists promote strategies of mass screening for primary identification of early neoplasms and aggressive follow-up after initial therapy. These may include surgical, chemo- or radiotherapeutic treatment, with repeated total body imaging with CT, MRI, or PET, sometimes in combination. Aggressive coronary atherosclerosis in a high-risk diabetic patient may be deadlier than most cancers. All our efforts are concentrated in detecting and treating the tip of the iceberg, the obstructive plaque causing ischaemia, a condition that certainly deserves treatment but represents the minority of the plaques causing acute events. A change in route may be advisable, if we do not want to end up like the 'Titanic'.

We must recognize that excellent care during the acute phase is often followed by suboptimal care in secondary prevention. The time to exploit the full potential of invasive coronary imaging to 'stage' the disease burden and better stratify long-term risk has arrived. Although complete eradication therapy in atherosclerosis is not possible, prolonged 'remissions' free from major cardiovascular events can be obtained with a combined approach of systemic pharmacological and focal mechanical therapy. Many aggressive liver or lung metastases are successfully treated with combination of local and systemic chemotherapy, alcoholization, or radiotherapy. Although controversial in the past, this approach guided by multidisciplinary oncological meetings with all the relevant specialists represented clearly improved survival.

Clinical cardiologists, cardiac imaging specialists, interventional cardiologists, dieticians, prevention, and rehabilitation specialists and, when appropriate, heart failure specialists, cardiovascular and bariatric surgeons, psychologists, diabetologists, hypertension specialists, and lipidologists have to review and discuss patients after an initial coronary event but also high-risk individuals before events develop. Prevention should cease being the boring task of out of hospital specialists and nurse practitioners with few contacts with other specialists. The multidisciplinary approach that has strengthened our approach in complex congenital heart disease, advanced heart failure, coronary revascularization, and transcatheter valve treatment should move to this neglected area. New diagnostic tests and pharmacological and interventional treatments hold the promise to make it the fastest growing field in modern cardiology.

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