

Contrast-free diagnosis and treatment of coronary artery disease guided by integrated cardiac imaging: concept and first clinical experience

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Abstract The use of iodinated contrast media (ICM) remains a potential hazard for patients undergoing diagnostic cardiac imaging and percutaneous coronary intervention. In particular patients with history of prior adverse reaction to a contrast agent are at a high risk in case of re-exposure, even if designated premedication is administered. Based on a patient with recurrent angina pectoris and history of systemic anaphylactic reaction to ICM, we describe the logical stepwise approach from diagnostic imaging to safe and successful imaging guided percutaneous coronary intervention without the use of contrast agent.

Keywords Anaphylaxis to iodinated contrast media · Cardiac imaging · IVUS-guided PCI

Introduction

Diagnosis and treatment of coronary artery disease (CAD) in patients with history of systemic anaphylactic reaction to iodinated contrast media (ICM) is challenging, since the risk of recurrent severe allergic reaction is high [1]. Furthermore, premedication can be ineffective and may have own side effects [2]. Thus, diagnostic and interventional

procedures in the given setting should favourably involve no contrast agents.

We report our first case of completely contrast agent-free diagnosis and treatment of CAD in a patient with history of a severe adverse event following ICM application.

Case report

A 74-year-old man with history of cancer-related gastrectomy, radiation and chemotherapy developed circulatory shock during routine follow-up computed tomography (CT), following administration of ICM. After successful hemodynamic stabilization, his ECG revealed transient ST elevation up to 2 mm in the antero-lateral leads and echocardiography displayed antero-septal apical hypokinesis correspondingly. Both findings disappeared upon intravenous application of nitrate. Cardiac enzymes showed only mild elevation with a peak creatine phosphokinase of 400 U/l 24 h after the event. During the following month, the patient reported chest oppression on effort in his daily life (CCS Class 3 angina) despite optimized medical therapy.

Exercise TI-201 (thallium) single-photon emission computed tomography (SPECT) revealed reversible perfusion defects in the apical and antero-septal left ventricular wall (Fig. 1a), indicating myocardial ischemia. For information on the rough anatomical course of the coronary arteries, non-contrast whole-heart magnetic resonance angiography (nc-MRA) was selected (Fig. 1b, c). In the next step, non-contrast ECG-gated cardiac CT (nc-CT) was performed to provide information on potentially hazardous coronary calcifications (Fig. 1d). Importantly, on cross-sectional assessment, calcification of the left anterior coronary artery (LAD) was located off-center (Fig. 1e).

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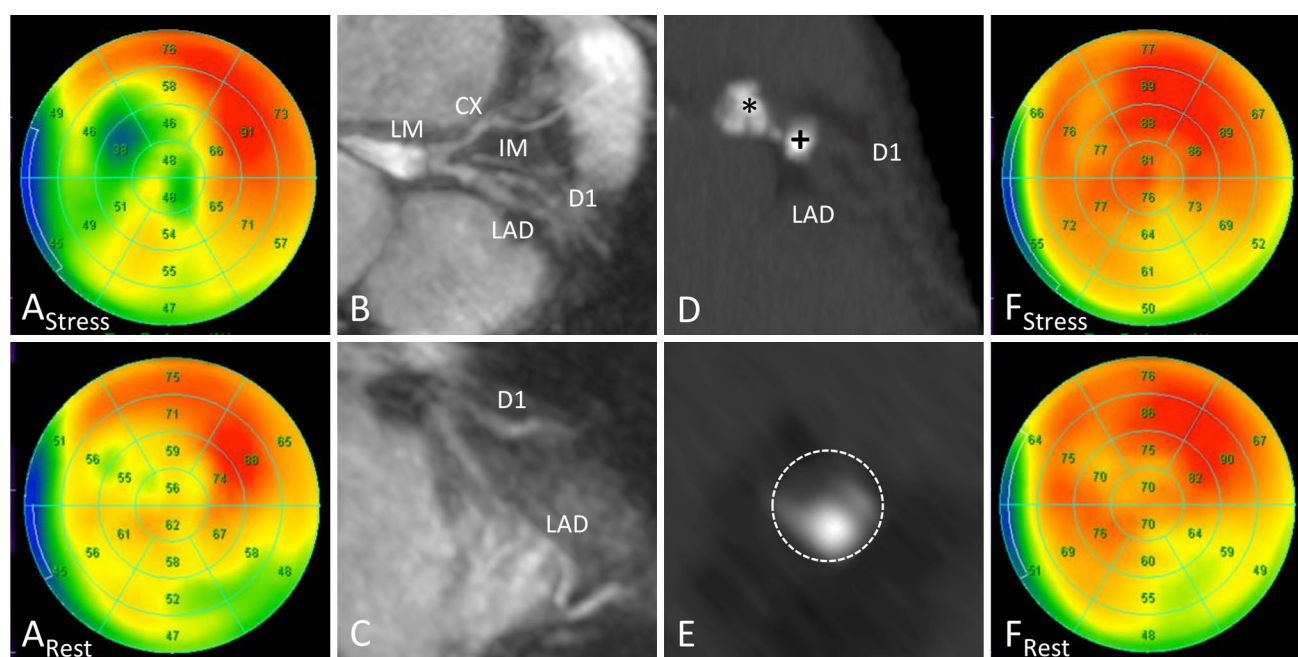


Fig. 1 **a** Exercise TI-201 (thallium) single-photon emission computed tomography (SPECT) revealed reversible perfusion defects in the apical and antero-septal left ventricular wall. **b** Contrast media-free MRA displays the anatomical course of the proximal left coronary artery, including left main (LM), circumflex (CX) and the left anterior descending artery (LAD) as well as intermediate (IM) and first diagonal branch (D1). **c** RAO cranial projection displays the LAD

with straight course until the mid portion, before continuing tortuous to the distal portion. **d** Contrast agent-free CT demonstrates calcification in the distal LM (asterisk) and the proximal LAD (plus). **e** Cross sectional view of the calcified LAD lesion demonstrates calcification only in the periphery of the vessel wall (dashed circle). **f** Follow-up exercise myocardial perfusion SPECT 1 month after stent implantation showed no residual ischemia

According to the integrated information of exercise SPECT, nc-MRA and nc-CT, the culprit lesion could be expected in the proximal LAD. Moreover, subject to location and calcification pattern, percutaneous coronary intervention (PCI) could be expected therapeutically effective with little probability of acute and late adverse events. Due to previous large surgeries, thoracic radiation therapy and the patient's anxiety towards another major surgery, PCI without the use of ICM was selected for treatment.

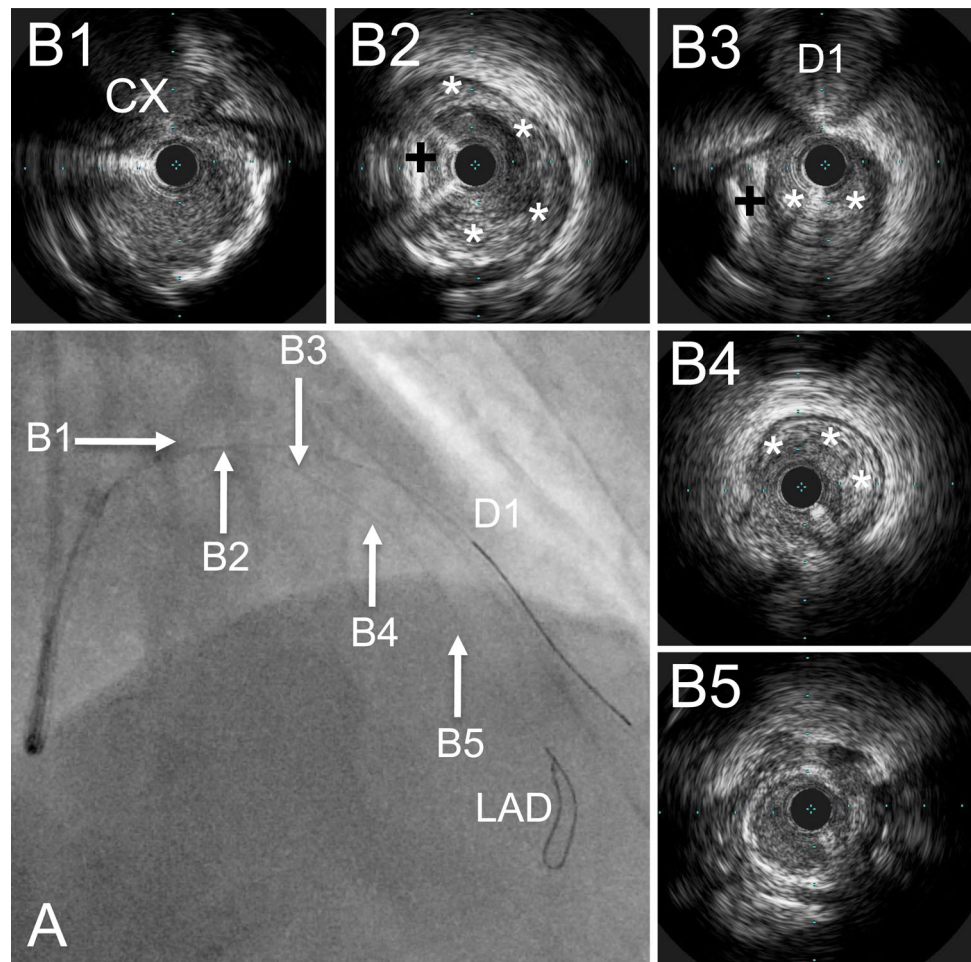
For maximum safety, ICM free PCI needed revised procedure strategies. The key points consisted of (1) choosing a guiding catheter easy to engage, (2) selection of the softest guide wire to prevent distal coronary injury, (3) stopping the procedure if the lesion cannot be crossed with a soft guide wire, and (4) use of intravascular ultrasound (IVUS) in addition to native fluoroscopy as previously described [3].

Initially, positioning the guiding catheter (6 Fr XB 3.0; Cordis Corporation, USA) at the ostium of the left coronary artery and advancing a guide wire (Runthrough extrafloppy; Terumo, Japan) into the large first diagonal branch (D1) was achieved by fluoroscopy imaging (supplementary material Video clip 1) and the anatomical information of nc-MRA (Fig. 1c). After localization of the LAD/D1

bifurcation by IVUS (Revolution; Volcano Corporation, USA), a second guide wire (Runthrough extrafloppy; Terumo Japan) could be smoothly advanced into the distal LAD (supplementary material Video clip 2). IVUS imaging, including a constant speed motorized pullback at 1 mm/s, was used to determine optimal stent diameter and length (Fig. 2; supplementary material Video clip 4). Accurate stent positioning in the proximal LAD without proximal protrusion or compromising the circumflex artery (CX) was achieved by IVUS imaging and fluoroscopic reference of another guide wire (Runthrough extrafloppy; Terumo, Japan) placed into the CX. Finally, two drug eluting stents (Xience V 3.0/28 mm and Xience V 2.5/15 mm; Abbott Vascular, USA) were implanted in the proximal to mid LAD (supplementary material Video clip 3). IVUS was repeated to carefully rule out significant residual stenosis and vessel injury such as dissection or hematoma (supplementary material Video clip 5). Since wire perforation in the distal vessels or distal embolization with mild to moderate flow impairment cannot be ruled out by IVUS, vital signs were monitored for another 15 min before the radial sheath was removed and the procedure finished.

At discharge, the patient had been clinically stable for 2 days without further ECG changes or rise of cardiac

Fig. 2 **a** Coronary angiogram in RAO cranial projection showing a guide wire in the left anterior descending artery (LAD) and in the first diagonal branch (D1). White arrows correspond to IVUS images B1–5. **b** IVUS images: B1 displays the first bifurcation with the ostium of the circumflex artery (CX), B2 depicts the proximal LAD with peripheral plaque burden (asterisk) and mild calcification (plus), B3 demonstrates that the D1 ostium is not affected by coronary artery disease, B3 and B4 picture the culprit lesion with eccentric plaque (asterisk) and mild calcification, limited to the vessel wall (plus), B5 shows the end of the stenosis, i.e. the designated distal stent landing zone



enzymes. Dual antiplatelet therapy (aspirin and clopidogrel) was set for at least 1 year. Follow-up exercise TI-201 SPECT 1 month after stent implantation showed no residual ischemia (Fig. 1f). In addition, the patient reported that his angina had completely disappeared.

Discussion

Up to the present date there is no consensus on how to manage patients with severe allergy to ICM who need coronary angiography. Different approaches have been suggested, including selection of an alternative contrast agent, premedication and desensitization [4].

Among the different ICM, low-osmolality contrast media have been proven less allergenic than high-osmolal contrast agents [5]. However, since the use of low-osmolal contrast media is already very common in vascular interventions [6], the choice of potentially less allergenic contrast media is limited. An iso-osmolal agent might have such favourable characteristics but explicit data are lacking and with the remaining iodine-based composition a

considerable risk of cross reactivity persists. As an iodine-free alternative, Gadolinium has been studied for use in patients with severe allergy to ICM undergoing coronary angiography. Its different chemical structure prevents cross reactivity with iodine-based contrast agents. However, despite the successful use for coronary angiography, several limitations have been identified. Apart from the generally lower image quality compared to ICM and the risk of induction of serious ventricular arrhythmias by intracoronary injection, the maximal recommended dose of 0.4 mmol/kg body weight limits its use, particularly if PCI is needed [4].

Prophylactic use of corticosteroids in combination with histamine blockers to reduce the risk of adverse ICM reactions has been recommended by expert panels [2, 7]. Nevertheless, the same authors also emphasize that especially in patients with history of severe reaction to ICM, premedication may not prevent occurrence of repeat events, as generalised reactions remain largely unpredictable [2, 7].

Desensitization of patients with history of anaphylactic reaction to ICM by repeated intravenous injections of the

contrast agent in increasing doses and concentrations has been successfully performed. However, sufficient evidence is lacking and the desensitization procedure in patients with history of anaphylactic reaction to ICM could also be risky [8]. Furthermore, desensitization needs extra time and is therefore not practicable in the setting of acute PCI.

In conclusion, the use of ICM for diagnosis and percutaneous revascularization of CAD is almost mandatory. Nevertheless, in the present case, latest advances in cardiac imaging allowed to stepwise determine the exact position as well as the characteristics of the culprit lesion. This detailed information allowed to carefully plan and finally carry out the intervention without use of ICM successfully.

Due to its wide availability, well-recognized accuracy in detecting significant CAD [9] and the dispensability of ICM, SPECT was selected for initial examination. Myocardial perfusion imaging clearly isolated the jeopardized myocardium and the corresponding coronary artery. Subsidary nc-MRA was performed to add anatomical information to the functional SPECT imaging. Native MRA not only allows non-invasive visualization of the main coronary arteries but also detection of significant coronary luminal narrowing with moderate sensitivity and high specificity [10]. Providing detailed information on coronary calcifications, nc-CT completed the non-invasive assessment. Acquaintance of extent and pattern of coronary calcification as assessed by nc-CT has recently been found to be a predictor for the complexity of PCI [11]. During PCI, IVUS allowed identification of position, size and number of stents needed for optimal treatment. At last, in a patient having already experienced cancer related large surgical procedures and thoracic radiation therapy, bypass surgery for a simple atherosclerotic coronary lesion could be avoided.

Despite being a valuable treatment option for selected cases, ICM-free PCI raises important safety concerns such as undetected vessel injury. Based on the information of noninvasive imaging and the general patient condition, a risk–benefit analysis should be carefully performed and discussed with the patient. PCI should only be considered if ischemia reduction in a corresponding myocardial territory and/or angina relief can be expected. If preinterventional imaging reveals lesion characteristics associated with more complex PCI (i.e. severe calcification, marked vessel tortuosity or multivessel disease), the indication for PCI should be reconsidered and other treatment options, as outlined earlier in this article, discussed in an interdisciplinary team. For maximal procedural safety, only soft, untapered guide wires and a safe guiding catheter should be used. Namely Amplatz-shaped catheters, deep intubation into the coronary artery and catheter manipulations have been identified as risk factors for coronary artery dissections [12] and should therefore be avoided. Final IVUS

assessment should be performed and carefully checked for dissections or flow-limiting hematomas. Because IVUS cannot rule out silent injuries in the distal vessel or distal embolization with mild to moderate flow impairment, the patient should be monitored for another 15–30 min before the sheath is removed and the procedure finished. If the intervention cannot be performed under the above mentioned security measures it should be stopped and other procedure options considered.

The substantial amount of technical effort for the comprehensive cardiac imaging, associated with additional radiation exposure and high costs in terms of time and money, may pose further limitations for our concept of contrast-free assessment and treatment of CAD. The growing use of medical imaging using ionizing radiation has raised concerns about patient safety and radiation risks [13]. However, current efforts to lower patient radiation exposure through optimized image acquisition protocols and modern scanners achieved impressive reductions while maintaining a high level of image quality and diagnostic performance [14]. In recent years, cardiac hybrid imaging is emerging as a combination of CT and myocardial perfusion imaging (SPECT or positron emission tomography, PET) in a single setting. In addition to the independent prognostic information through morphological and functional imaging criteria, cardiac hybrid imaging provides useful data for the planning of complex revascularization procedures [15] and may therefore further enhance the concept of contrast-free assessment and treatment of CAD.

Conclusion

Imaging and revascularization of the coronary arteries without the use of contrast agent is feasible and can be considered in patients with history of severe adverse reaction to ICM. This is the first case to report the logical stepwise approach from diagnosis and planning to successful PCI without application of contrast media, using integrated functional and anatomical information of IVUS, SPECT, nc-MRA and nc-CT.

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