Interventional Cardiology

Research highlights in interventional cardiology

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Is atrial fibrillation after coronary artery bypass grafting dependent on pulmonary vein triggers?

Evaluation of: Kiaii B, Fox S, Chase L *et al.* Postoperative atrial fibrillation is not pulmonary vein dependent: results from a randomized trial. *Heart Rhythm* 12, 699–705 (2015).

A third of patients undergoing cardiac surgery suffer from postoperative atrial fibrillation (POAF). POAF leads to an increased morbidity (stroke, bleeding, heart failure) and mortality (twofold increase in cardiac mortality). Therefore, POAF is a major cause of complications after cardiac surgery. Given its relevance, little is known about the mechanistic background and there is no widely accepted prevention as well as treatment strategy for POAF.

Kiaii *et al.* analyzed in this study the role of concomitant pulmonary vein isolation (PVI) during on-pump coronary artery bypass grafting (CABG) in patients without previously known atrial fibrillation (AF). The study is based on the concept, that especially in patients with paroxysmal AF (not related to cardiac surgery), the pulmonary veins are the dominant trigger side and PVI leads to a high arrhythmia-free survival in these patients. Therefore, the authors hypothesized a similar importance of pulmonary vein triggers in POAF.

For this purpose, they randomized a total of 175 patients to CABG + PVI versus CABG without PVI and analyzed the burden of POAF >5 min. The PVI was done with an epicardial bipolar radiofrequency clamp (Cardioblate BP2, Medtronic, MN, USA) with confirmation of an exit block from the pulmonary vein to the left atrium. PVI was achieved in 92% of patients.

The baseline characteristics were comparable in both groups. The $CHADS_2$ score was surprisingly low (median 1), but similar in both groups. As expected, the operation time was longer in the CABG + PVI group (259 vs 234 min; $p < 0.001$). Importantly, the portion of possibly proarrhythmic postoperative inotropic drug support was similar in both groups.

The results were surprising: 37% in the CABG + PVI group versus 36% in the CABG without PVI developed POAF (defined as AF > 5 min). Complication rates were comparable in both groups.

In addition, the incidence of AF 30 days and 6 months postoperatively was also similar (in both groups nearly no patient suffered from AF at these time points).

Therefore, in this study pulmonary vein triggers seem to be irrelevant for POAF. The mechanistic background of POAF may be different from AF not related to cardiac surgery. Thus, a prophylactic PVI in patients without a history of AF before cardiac surgery is not recommended at this time point. Currently, beta blockers (decrease POAF prevalence from 39 to 31%) or amiodarone (decrease from 30 to 16% when given 6 days before surgery) remain so far the only possibilities to prevent POAF.

TOTAL: a randomized trial of routine thrombus aspiration in STEMI

Evaluation of: Jolly SS, Cairns JA, Yusuf S *et al.* Randomized trial of primary PCI with or without routine manual thrombectomy. *N. Engl. J. Med.* 372, 1389–1398 (2015).

Manual thrombus aspiration with aspiration catheters can reduce thrombus burden

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in acute coronary syndromes and possibly prevent no-reflow and microvascular obstruction after macrovascular recanalization. There is still conflicting evidence regarding the routine use of thrombectomy devices from different trials. While in the 2008 TAPAS trial (1071 patients) thrombectomy was associated with improved myocardial blushing and blushing in turn was associated with survival, the more recent 2014 TASTE (7244 pts) trial found no evidence in support of thrombus aspiration.

The multinational TOTAL trial included 10,732 patients with STEMI undergoing primary PCI in 87 hospitals and randomized them in a 1:1 ratio to either PCI alone (control group) or routine thrombectomy with the Medtronic Export catheter followed by percutaneous coronary intervention (PCI). Bailout thrombus aspiration was allowed in the PCI alone group and was performed in 355 patients (7.1%). The primary outcome of the study was the combination of death from cardiovascular causes, recurrent myocardial infarction, cardiogenic shock or new NYHA IV heart failure within 180 days of the procedure. The primary safety outcome was stroke within 30 days.

Both groups were quite similar with slightly higher time from symptom onset to PCI in the thrombectomy group (128 vs 120 min). As expected, procedural time was about 4 min longer with the use of thrombus aspiration than with PCI alone (39 vs 35 min ; $p < 0.001$).

At 180 days, the primary outcome occurred in 6.9% in the thrombectomy group and in 7.0% in the PCI alone group ($p = 0.86$). No relevant differences with respect to the secondary outcomes were reported, except for the clinically irrelevant parameter resolution of ST changes. There was no statistically significant difference in no-reflow rates (2.4 vs 2.8%; $p = 0.28$). Also in prespecified subgroups, most importantly those with high thrombus burden, there was no advantage of thrombectomy.

In terms of the safety end point, stroke within 30 days occurred significantly more frequently in the thrombectomy group compared with the PCI alone group (0.7 vs 0.3%; HR 2.06; $p = 0.02$) with the

Table 1. Comparison of the patient characteristics and outcome data of the TASTE and TAPS trial.

Trial	TOTAL	TASTE	TAPAS
Patients	10732	7244	1071
Inclusion criteria	STEMI with PCI within 12 h of onset, no prior fibrinolysis or CABG	STEMI with primary PCI planned within 24 h of symptom onset	Possible STEMI with primary PCI within 12 h of onset
Age (intervention group)	61 ± 11.8	66.5 ± 11.5	63 ± 13
Male	76.8%	75.1%	67.9%
Intervention	Routine manual thrombectomy vs PCI alone with bailout thrombectomy only (7.1%).	Routine manual thrombectomy vs PCI alone (4.9% thrombectomy rate)	Routine manual thrombectomy vs PCI alone (crossover rate not reported).
Study design	Multicenter, randomized open trial with blinded adjudication.	Multicenter, randomized registry study	Single center, prospective randomized open trial with blinded adjudication
Sponsor	Investigator initiated, public plus industry funding.	Investigator initiated, public plus industry funding.	Investigator initiated with industry grant.
Primary outcome	Combination of cardiovascular death, recurrent MI, cardiogenic shock, NYHA IV HF within 180 days.	All-cause mortality	Myocardial blush grade 0 or 1 post procedure.
Result	6.9 vs 7.0%; p = 0.86	2.8 vs 3.0%; p = 0.62	17.1 vs 26.3%
No-reflow	2.4 vs 2.8%; p = 0.28		
Stroke	0.7 vs 0.3% at 30 days	0.5 vs 0.5%	Not reported
Catheters	Export	Eliminate, Export, Pronto (others allowed)	Export
Result interpretation (study authors)	Routine thrombectomy does not reduce clinical events and is associated with an increased rate of stroke	No difference in mortality or other outcomes between thrombectomy and PCI alone at 30 days in patients presenting with STEMI	Manual thrombus aspiration results in improved myocardial blushing and clinical outcome

Table 2. Comparison of the larger trials dealing with CT-A in acute chest pain patients.

Trial	PROMISE	ROMICAT-II	ROMICAT-I	FACTOR-64	NXT
Number of patients	10,003	1000	368	900	254
Inclusion criteria	Symptomatic outpatients with further evaluation for CAD deemed necessary	Age 40–74, presenting to ED (no prior cardiac disease)	Patients presenting to ED with acute chest pain without prior cardiac disease	Asymptomatic patients with diabetes for at least 3 years duration	
Age	60.8	54	53	61	64
Male%	47%	52	61	52	64
CAD risk	Diamond and Forrester 53.4%	Not given	94% low TIMI risk, 5% intermediate	Framingham risk < 10; 10–20; >20%: 349; 420; 130	D &F score 57.8%
Noncardiac pain	10.7%	85%	92%	Asymptomc	5%
Design	Multicenter (193 US), randomized comparative effectiveness design	Randomized, controlled, multicenter	Single-center, observational cohort study	Single-center randomized study	Prospective multicenter diagnostic trial
Study test	64 slice or greater CTA	64 slice CTA, on-site reading	64 slice CTA	64 slice CTA	64 slice CTA + FFRCT
Control group	Functional testing (nuclear, stress echo, stress ECG)	Standard evaluation	None; diagnostic study	Standard care	Invasive angiography + FFR
End point	MACE within follow-up period	Length of stay	Sensitivity for ACS	All-cause mortality, MI, UA, hospitalization over 4 years	Correlation of invasive FFR and CR-FFR
Result	3.3 (CTA) vs 3.0% (FT) MACE during follow-up	CTA 23.2 vs 30.8 h of stay	Sensitivity 77% for stenosis, PPV for stenosis 35%; NPV 98%	6.2 vs 7.6% p = 0.38	Sensitivity 85%, specificity 79% vs ICA with FFR specificity of regular CTA: 34%
CT scanner	Multivendor		Siemens Sensation 64	Toshiba Aquilion 64	Multivendor
Radiation	12.0 vs 10.1 mSv	14.3 vs 5.3 mSv	Not given	Not given	Not given
Rate of invasive angiography	12.2 vs 8.1%	12 vs 8%	20 of 31 patients with ACS	13.3 vs 5.1% PCA 6 vs 1.8%	All patients
Conclusion	In symptomatic patients a CTA-based strategy was not associated with better clinical outcomes over 2 years	Improved efficiency of clinical decision without harm	Coronary CTA may improve management of patients with acute CP in ED	Among asymptomatic diabetic CTA did not reduce clinical events at 4 years follow-up	FFR CT increases specificity compared with regular CTA.
Comment	Largest study showing no benefit of CTA vs functional testing.	Both groups had virtually no events, length of stay unusually high for low risk group from European perspective	At an average length of stay of 40.5 h in a low risk group, there seem to be many better ways to improve management than CTA. CTA only ruled out ACS in 50.3% of this cohort	Yet another negative screening trial.	Study testing an interesting concept which may improve the value of CTA, but also demonstrates the current limits of CTA in terms of specificity and sensitivity. A patient management trial is ongoing
Publication	*N. Engl. J. Med.* 372, 1291–1300 (2015)	*N. Engl. J. Med.* 367, 299–308 (2012)	*J. Am. Coll. Cardiol.* 53(18),1642–50 (2009)	*JAMA* 312(21), 2234–2243 (2014)	*J. Am. Coll. Cardiol.* 63(12), 1145–55 (2014)

event rates separating very early in the course, but with higher event rates also occuring late after thrombus aspiration.

When interventional trials are not successful, the most common explanations provided are inadequate material or operator experience. The results of this trial cannot be easily disregarded and are likely to change guideline recommendations.

Nevertheless, the results of this trial should not be interpreted as proof that manual thrombus aspiration *per se* does not work, but rather that it may not be necessary in most cases because angioplasty alone will do the job. In cases where PCI is not successful, however, thrombectomy should be considered and indeed can sometimes save the day as a bailout procedure, associated with a very low incidence of stroke. The results of this trial therefore are not the end of thrombus aspiration in case of an MI, but rather do not recommend routine use in every patient.

PROMISE: trial of CTA versus functional testing in chest pain

Evaluation of: Douglas PS, Hoffmann U, Patel MR *et al.* Outcomes of anatomical versus functional testing for coronary artery disease. *N. Engl. J. Med.* 372, 1291–1300 (2015).

Current management of patients with chest pain involves ECG, biomarkers like high-sensitive troponins and functional testing. While this strategy has proven its effectiveness, it may be time-consuming depending in particular on the availability of services for functional testing. Whether the use of modern CT angiography (CTA) may lead to a better clinical outcome remains to be established. While the good sensitivity of CTA for coronary artery disease (CAD) has been shown, use of CTA screening has not been shown to result in improved outcomes in patients with diabetes (FACTOR-64). The PROMISE trial is the largest trial ever performed to study the usefulness of CTA for the detection of significant CAD. This trial was designed to test not only the diagnostic properties of CTA but also the influence of CTA results on important patient outcomes. So far, it is the only adequately powered study to address this issue.

In this comparative effectiveness trial patients without prior cardiac disease and new onset chest pain were assigned to either CTA or functional testing with myocardial perfusion imaging, stress echocardiography or exercise ECG. The primary study end points were major cardiovascular events and major procedure-related complications and testing. Clinical events were adjudicated by an independent and blinded committee based on predetermined definitions.

Results

At total of 10,003 patients were included and followed for a median of 25 months. The patients had a relatively high cardiovascular risk with a mean Diamond and Forrester risk score of roughly 53% in both groups. In the functional test cohort, nuclear stress testing was performed in 68%, stress echocardiography in 22% and exercise ECG in 10%.

During follow-up the primary outcome occurred in 3.3% of patients in the CTA group and in 3.0% of patients in the functional testing (FT) group, which exceeded the prespecified boundary for noninferiority of CTA versus FT.

The rate of invasive coronary angiography was higher at 12.2% in the CTA group versus 8.1% in the FT group. Also the overall radiation exposure in the CTA group was higher than in the FT group (12.0 vs 10.1 mSv; $p < 0.001$), despite the high utilization of nuclear stress testing. There were fewer coronary angiographies showing no CAD in the CTA group.

The results of the trial demonstrate that CT angiography does not improve long-term clinical outcomes in patients with new-onset chest pain, but causes more radiation exposure and increases the number of invasive coronary angiographies. Depending on the clinical setting it may be used as a substitute for functional testing. When equally effective alternatives with zero radiation exposure like stress echocardiography are available, the use of a diagnostic test like CTA seems only warranted in individual cases not qualifying for alternative modalities. Problems of local availability and patient management considerations do not currently justify the routine use of such a modality. Instead, stress tests are recommended with the advantage of zero radiation.

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