OCT to optimize results of PCI in patients with non-ST-ACS

Results of the multicenter, randomized DOCTORS study Circulation 2016

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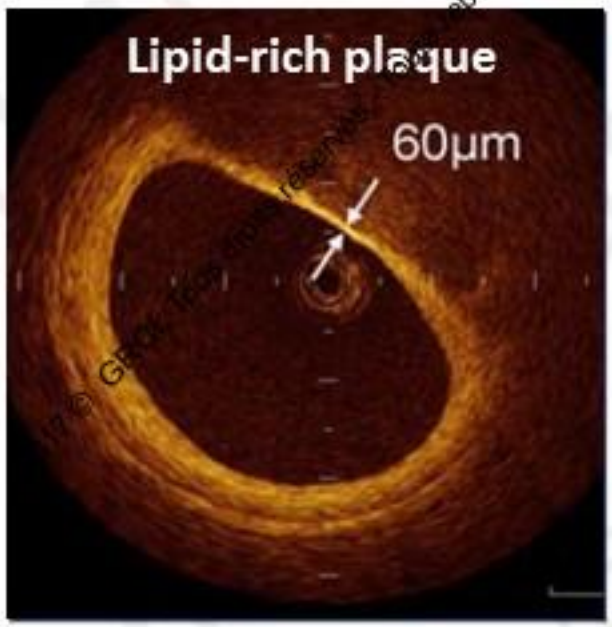
DÉCLARATION DE LIENS D'INTÉRÊT AVEC LA PRÉSENTATION

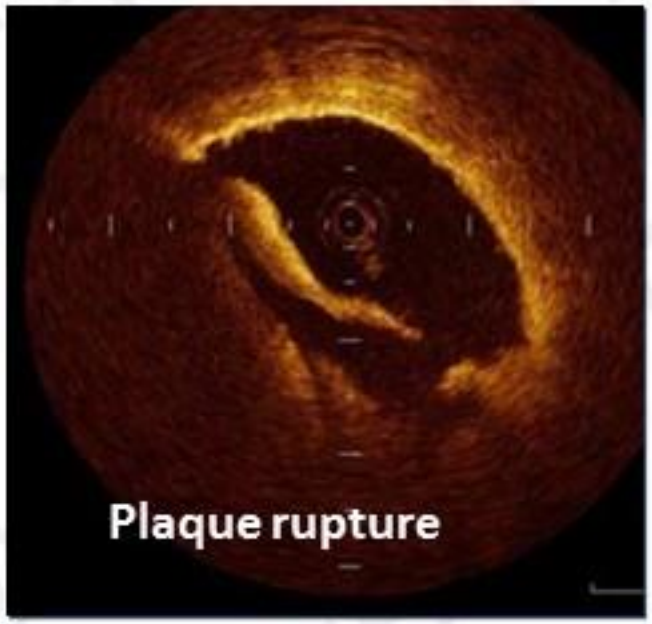
Intervenant : Dr Nassim BRAIK, Paris

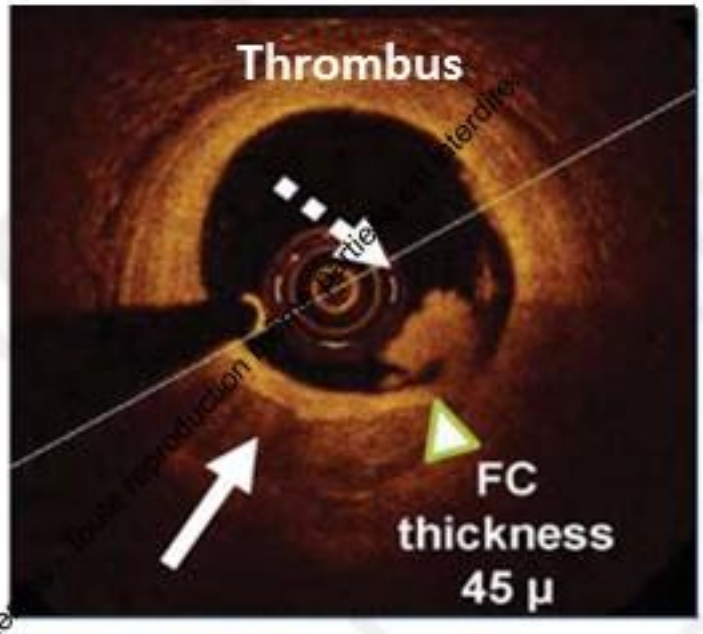
☑ Je n'ai pas de lien d'intérêt à déclarer.

Background

- OCT offers potential advantages over angiography :
  - To identify plaque morphologies associated with worse prognosis [1-3] in ACS pts



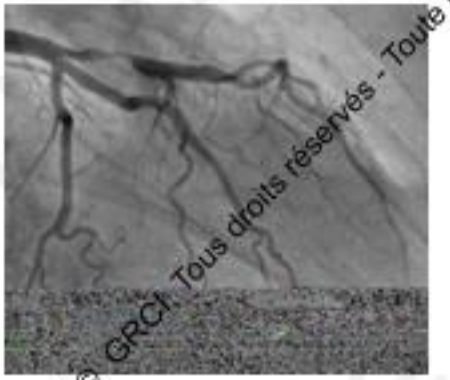


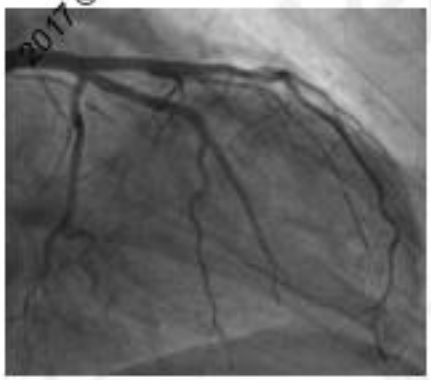


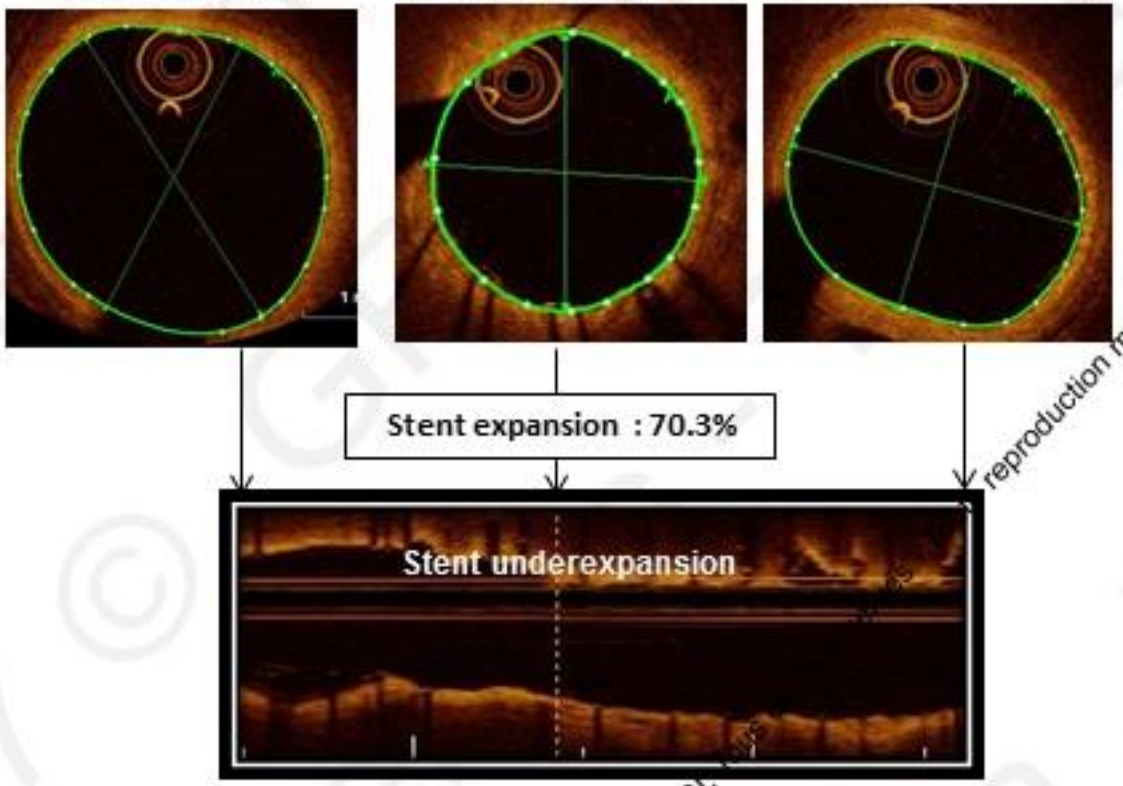
[1]Niccoli G et al. Eur Heart J. 2015;36:1377-1384. [2]Vergallo R et al. Am Heart J. 2014;167:59-67. [3]Porto I et al. Circ Cardiovasc Interv. 2012;5:89-96,S81-86.

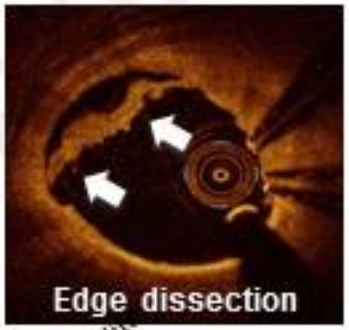
Background

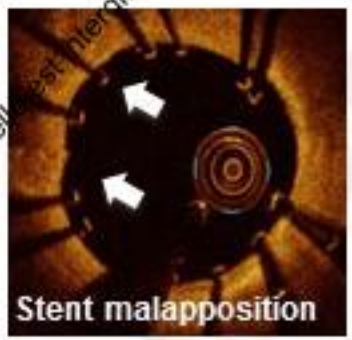
- OCT offers potential advantages over angiography :
  - To assess postprocedural results

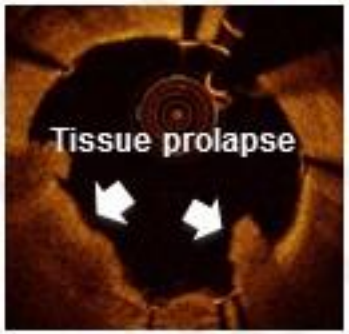












Background

- OCT offers potential advantages over angiography :
  - To identify plaque morphologies associated with worse prognosis [1-3] in ACS pts
  - To assess postprocedural results
- Additional information yielded by OCT imaging during PCI impacts on physician decision-making in two-thirds of cases .
- It remains to be investigated whether the use of additional interventions prompted by OCT findings will translate into a benefit in procedural outcome.
- In this setting, randomized data investigating the utility of OCT over angiography alone to guide PCI are lacking , specifically in patients with NSTE-ACS.

[1]Niccoli G et al. Eur Heart J. 2015;36:1377-1384. [2]Vergallo R et al. Am Heart J. 2014;167:59-67. [3]Porto I et al. Circ Cardiovasc Interv. 2012;5:89-96,S81-86.

Wijns W et al. Eur Heart J. 2015;36:3346-3355. Waksman R et al. Eur Heart J. 2015;36:3356-3358. [8]awlani NN et al. JACC Cardiovasc Imaging. 2015;8:1306-1308.

Aim of the Study

The DOCTORS study aimed to evaluate :

- whether the use of OCT during PCI would provide useful clinical information beyond that obtained by angiography alone
- whether this information would modify physician decision-making
- and impact on the functional result of angioplasty as assessed by **fractional flow reserve** (FFR) measured after stent implantation in a lesion responsible for NSTE-ACS.

Participating Centers

- Conducted in 9 university and general (non-academic) hospitals in France
  - (1) University Hospital Jean Minjoz, Besancon, (Pr N. Meneveau)
  - (2) University Hospital Gabriel Montpied, Clermont-Ferrand, (Pr P. Motreff)
  - (3) Institut Mutualiste Montsouris, Cardiology, Paris, (Dr C. Caussin)
  - (4) University Hospital of Strasbourg, (Pr P. Olhmann)
  - (5) Hospital Belfort-Montbeliard, (Dr Y. Lefrançois)
  - (6) General Hospital, Cardiology, Chambéry, (Dr V. Descotes Genon)
  - (7) Hospital Pitie-Salpétriere, Paris, (Pr G Montalescot)
  - (8) Centre Hospitalier Annecy-Genevois, (Dr L. Belle)
  - (9) University Hospital of Lille (Pr E. Van Belle)

Study Design

Study Design

- Randomized, prospective, multicenter, open label trial (registered on ClinicalTrials.gov under the identifier NCT01743274)
- Performed in 9 university and general (non-academic) hospitals in France
- Study design previously published (Am Heart J 2014;168:175-181.)

Funding

- The DOCTORS study was funded by the French government's national hospital research program (Programme Hospitalier de Recherche Clinique 2013).

Meneveau N et al. Am Heart J 2014;168:175-181.

Patient Population

Inclusion criteria:

- Patients aged 18 to 80 years, admitted for ACS;
- Chest pain at rest lasting for ≥ 10 min in the previous 72 hrs;
- **and** ≥ 1 of the following two criteria:
  - (i) new ST segment depression ≥1 mm or transitory ST segment elevation (<30 minutes) (≥1 mm) on ≥ 2 contiguous leads of the ECG;
  - or (ii) elevation (>upper limit of normal, ULN) of cardiac enzymes (CK-MB, Troponin I or T);
- **and** presenting an indication for PCI with stent implantation of the target lesion (single lesion on the culprit artery without diffuse disease on the same vessel) considered to be responsible for the ACS.
- **and** written informed consent.

Patient Population

Exclusion criteria :

- Left main disease;
- In-stent restenosis;
- Presence of CABG; cardiogenic shock;
- Severely calcified or tortuous arteries;
- STEMI;
- **≥ 1 other lesions considered angiographically significant or non-significant diffuse disease located on the target vessel;**
- **Severe renal insufficiency (eGFR ≤30 mL/min);**
- Bacteremia or septicemia;
- Severe coagulation disorders;
- Pregnancy.

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Study Endpoints

Primary endpoint :

- Fractional flow reserve (FFR) measured at the end of the procedure (average of 3 consecutive measures)

Secondary endpoints :

1. Procedural complications defined as occurrence of no reflow, coronary perforation, occlusive dissection, spasm, or stent occlusion.
2. Peri-procedural (type 4a) MI as defined by the 3rd Universal Definition of MI[1].
3. Identification of a threshold value for quantitative OCT findings that best predicts an FFR value >0.90.

Safety Endpoints :

1. Acute Kidney Injury (AKI) defined as an absolute increase in serum creatinine of ≥0.5 mg/dL from baseline [2].
2. Duration of the procedure; fluoroscopy time; quantity of contrast media used, and radiation dose delivered.

[1]Thygesen. EHJ. 2012;33:2551-2567. [2]KDIGO. Kidney Int Suppl. 2012;2:1-138.

Sample Size Calculation

The sample size was calculated based on the following assumptions:

- Average FFR value after stent implantation of 0.92*
- Standard deviation of 0.0714*
- Under the hypothesis that the use of OCT would improve FFR by 0.03 units
- Alpha risk of 5%
- Beta risk of 10%
- 115 patients required in each arm
- To account for attrition, technical failures or images unsuitable for analysis, an additional 5 patients were included in each group
- Total : 240 patients (120 in each group)

*Pijls. NH et al. Circulation 2002;105:2950-54. Meneveau. Am Heart J 2014;168:175-181.

Pts fulfilling the inclusion criteria

Randomization

OCT-guided group

OCT run before PCI :
- quantitative OCT measures
- plaque morphology, presence of thrombus or calcifications

- Choice of stent length and diameter based on quantitative OCT measures
- IIb/IIIa inhibitors, thrombectomy, or rotational atherectomy considered in case of thrombus or calcifications

OCT run after stent implantation :
- quantitative OCT measures
- presence of thrombus, edge dissection, prolapse, optimal lesion coverage, stent malapposition or underexpansion.

- Additional balloon overdilation to be performed if stent underexpansion*
- Additional stent implantation(s) to be performed if incomplete lesion coverage.
- Management of malapposition & edge dissection at operator's discretion.

Several OCT runs could be performed. The run with a satisfactory result considered as the final run.

Final FFR measurements**

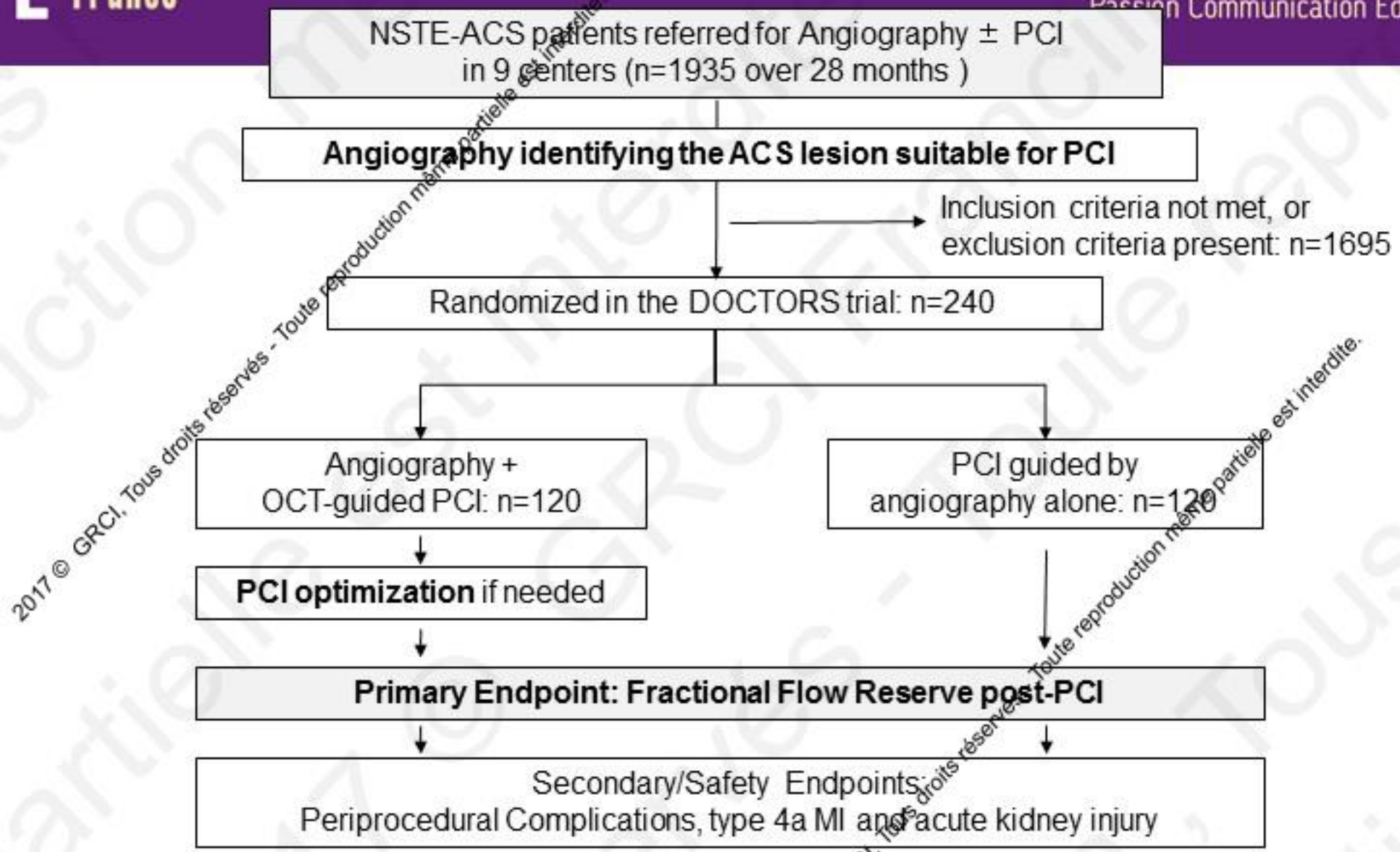
Angiography-guided group

PCI guided by fluoroscopy alone, performed before and after stent implantation according to standard of care

Final FFR measurements**

*Stent under-expansion was defined as a ratio of in-stent MLA to reference lumen area ≤80%.

**once the operator considers the result of PCI to be optimal

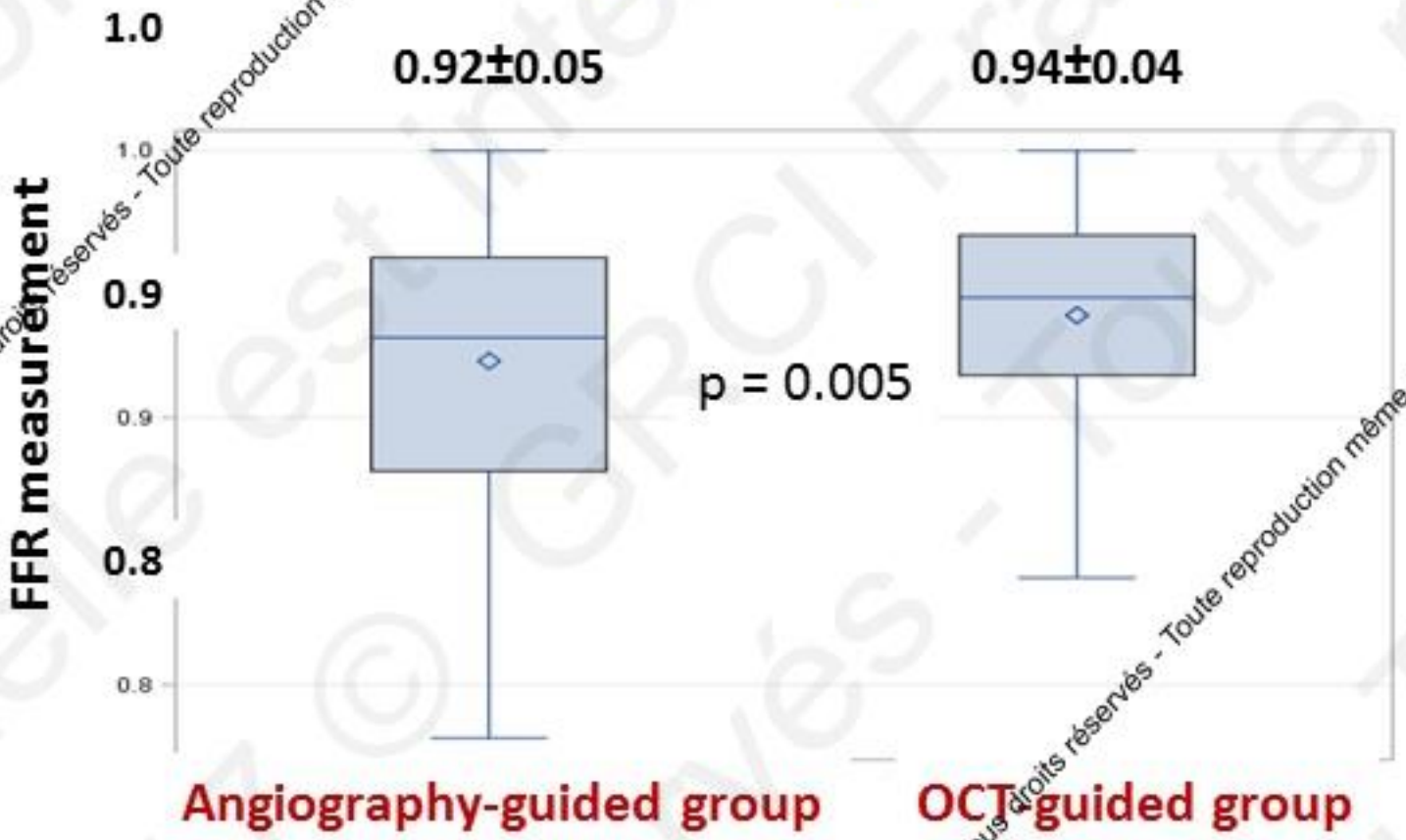


Study Population

Variable	Overall (N=240)	Angio-guided group (n=120)	OCT-guided group (n=120)	P value
Age, years	60.5±11.4	60.2±11.3	60.8±11.5	0.72
Male sex	186 (77.5%)	91 (75.8%)	95 (79.2%)	0.53
Diabetes mellitus	45 (18.8%)	19 (15.8%)	26 (21.7%)	0.25
Hypercholesterolemia	115 (47.9%)	56 (46.7%)	59 (49.2%)	0.70
Hypertension	117 (48.8%)	50 (41.7%)	67 (55.8%)	0.03
Troponin, µg/L	0.79 [0.2; 2.5]	1.1 [0.2; 4.1]	0.54 [0.2; 1.7]	0.33
Vessels diseased (1/2/3)	166/54/20	88/24/8	78/30/12	0.28
IRA (RCA/LCX/LAD)	70/54/116	32/28/60	38/26/56	0.63

Meneveau N et al. Circulation 2016 Sep 27; 134 (13); 906-17.

Primary Endpoint : FFR



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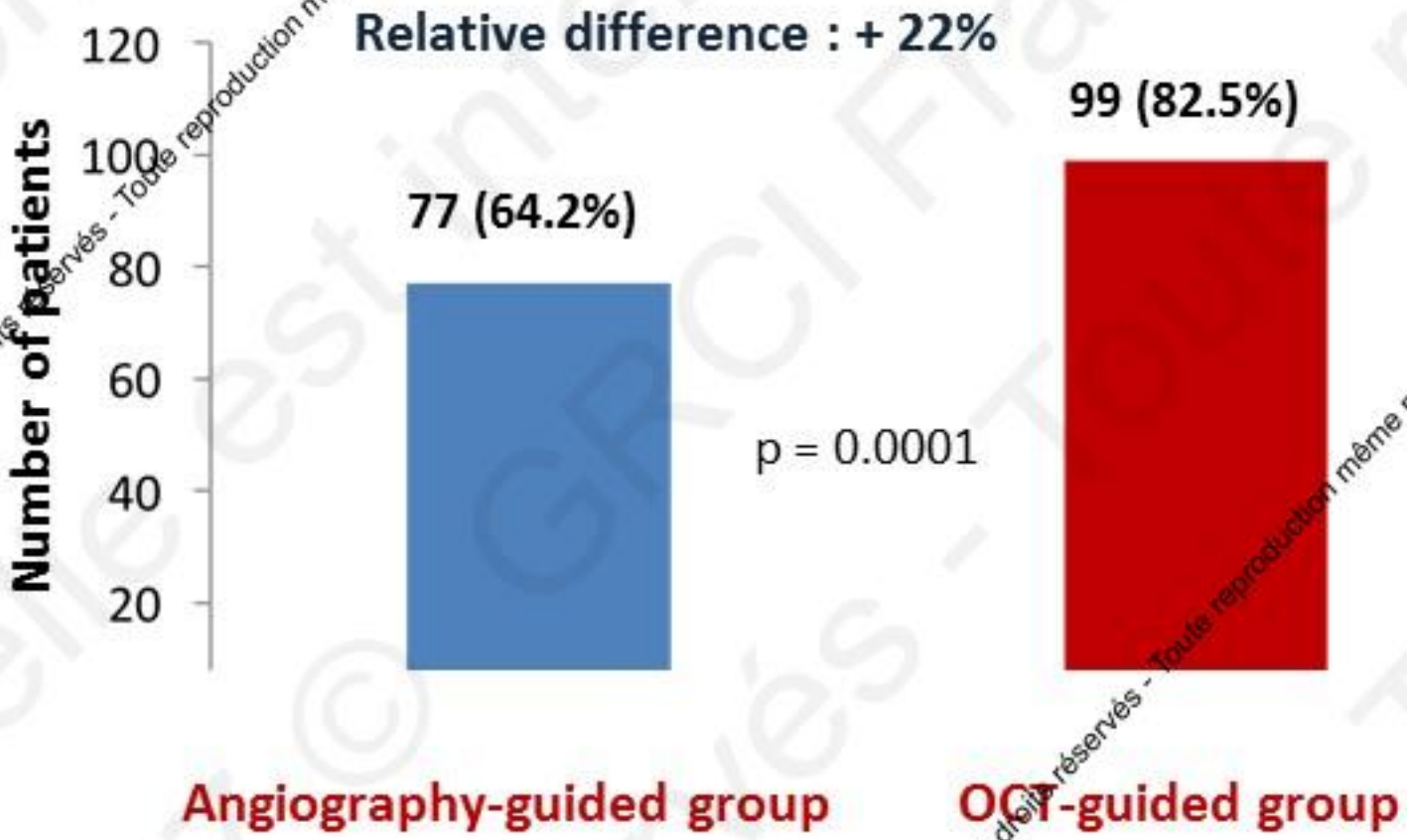
Number of Patients with post-PCI FFR > 0.90



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Impact of pre-PCI OCT

Variable	Angio-guided group (n=120)	OCT-guided group (n=120)	P value
Presence of thrombus	56 (47%)*	83 (69%)†	0.0004
Presence of calcifications	11 (9%)*	55 (45.8%)†	< 0.0001
Plaque rupture	-	44/88 (50%)†	-
Lipid-rich plaque/fibrous plaque	-	92/28 (77%/23%)†	-
Procedural strategy			
- Aspiration thrombectomy	4 (3.3%)	2 (1.7%)	0.41
- GP IIb/IIIa inhibitors	43 (35.8%)	64 (53.3%)	0.007
- Stent length, mm	17.3±5.5	17.9±5.6	0.44
- Stent diameter, mm	3.11±0.41	3.11±0.41	0.94

*by visual assessment. †as visualized by OCT.

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Treatment prior to and during PCI

Pre-Procedure	Angio-guided group (n=120)	OCT-guided group (n=120)	P value
Loading dose of P2Y12 inhibitor	92 (77%)	97 (81%)	0.43
Loading dose of aspirin	91 (76%)	95 (79%)	0.54
Anticoagulant during PCI			
- Unfractionated heparin	111 (92.5%)	112 (93%)	0.95
- Enoxaparin	6 (5%)	5 (4.5%)	
- Bivalirudin	3 (2.5%)	3 (2.5%)	
Periprocedural GP IIb/IIIa inhibitor	43 (36%)	63 (53%)	0.007

Impact of post-PCI OCT

	Angio-guided group (N=120)	OCT-guided group (N=120)	P value
Stent malapposition	–	38 (32.0%)†	--
Stent under-expansion	13 (10.8%)*	50 (42%)†	<0.0001
Tissue protrusion	–	95 (79%)†	--
Incomplete lesion coverage	20 (17%)*	24 (20%)†	0.51
Edge dissection	5 (4%)*	45 (37.5%)†	<0.0001
Procedural optimization	27 (22.5%)	60 (50%)	<0.0001
- Post-stent overdilation	15 (12.5%)	52 (43%)	<0.0001
- Additional stenting	22 (17.5%)	32 (27%)	0.09
- Total stent length, mm	20.4±9.0	21.9±9.3	0.17

*by visual assessment. †as visualized by OCT.

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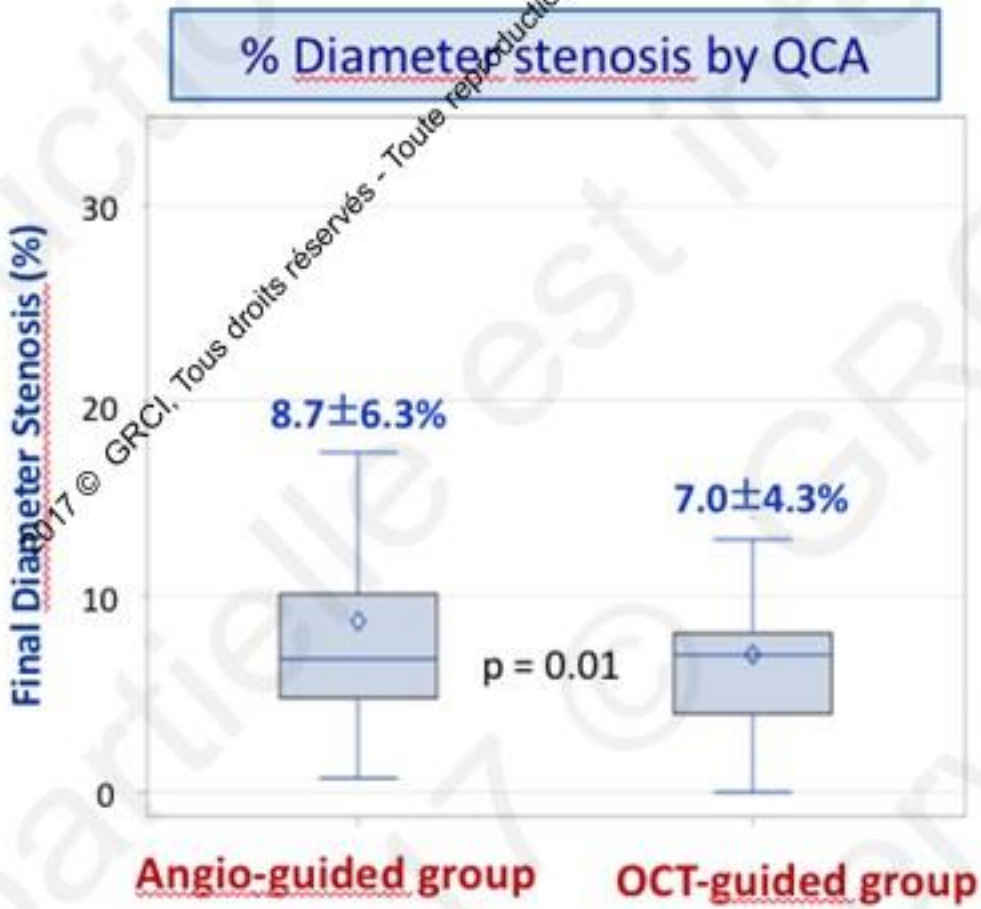
Quantitative angiographic findings

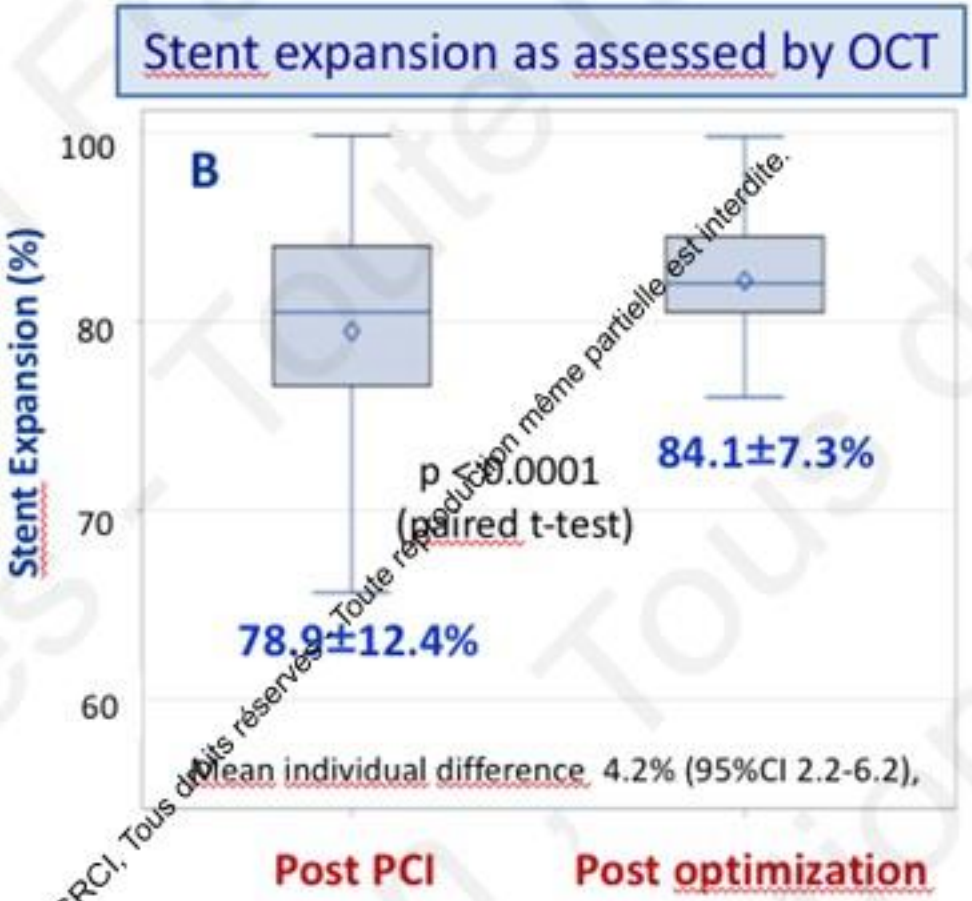
Variable	Angio-guided group (n=120)	OCT-guided group (n=120)	P value
Quantitative Findings Pre-Procedure			
Reference diameter, mm	2.88±0.39	2.81±0.41	0.18
MLD, mm	0.87±0.29	0.81±0.30	0.12
Diameter stenosis, %	69.3±9.4	71.3±9.9	0.12
Lesion length, mm	13.5±6.0	13.7±6.4	0.80
Quantitative Findings Post-Procedure			
Reference diameter, mm	3.16±0.37	3.13±0.41	0.48
MLD, mm	2.90±0.42	2.89±0.40	0.82
Diameter stenosis, %	8.7±6.3	7.0±4.3	0.01

Quantitative OCT findings

Variable	Pre-Stenting	Immediately post-stenting	Post-OCT optimization	P value*
Reference diameter, mm	2.92±0.53	3.10±0.45	3.11±0.48	0.27
MLD, mm	1.21±0.33	2.79±0.46	2.84±0.43	0.001
Diameter stenosis, %	58.4±10.9	9.5±6.1	8.4±3.9	<0.0001
Reference area, mm²	7.0±2.23	7.62±2.42	7.72±2.43	0.10
MLA, mm²	1.28±0.71	5.99±2.11	6.41±1.99	<0.0001
Area stenosis, %	81.1±9.82	21.1±12.4	15.9±7.3	<0.0001

Impact of post-PCI OCT





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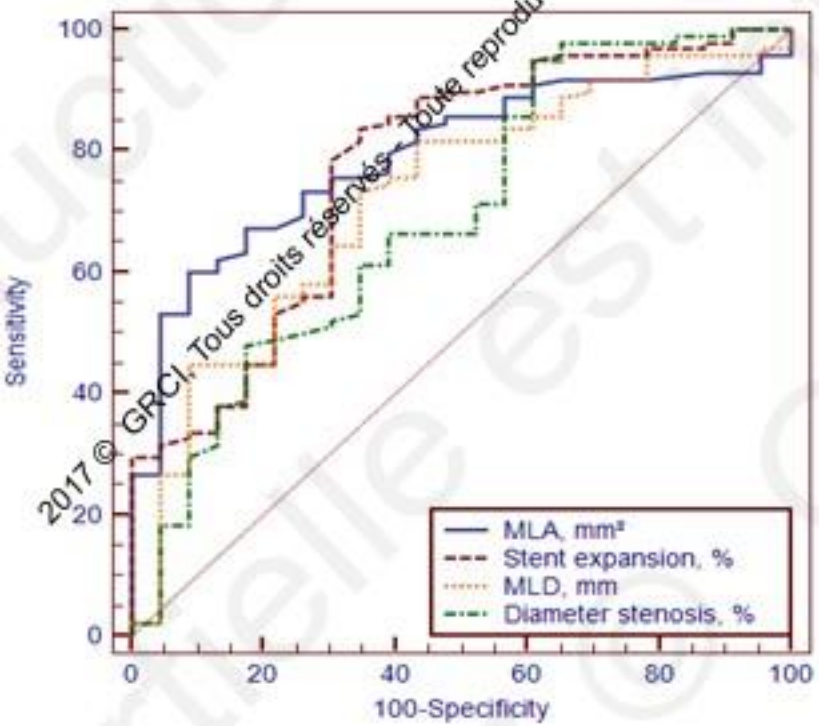
Quantitative OCT parameters that best predict FFR >0.90



	AUC 95%CI	Youden index criterion	Se (%)	Spe (%)
MLA	0.79 [0.71 ; 0.86]	>5.44 mm^2	91.3	60.2
Stent expansion	0.77 [0.69 ; 0.84]	>79.4 %	83.7	65.2
MLD	0.72 [0.63 ; 0.80]	>2.73 mm	65.2	73.5
Diam. Stenosis	0.69 [0.60 ; 0.77]	≤11.5 %	39.1	94.9

Secondary and safety outcomes

Variable	Angio-guided group (n=120)	OCT-guided group (n=120)	P value
Type 4a myocardial infarction	40 (33%)	48 (40%)	0.28
Procedural complications	7 (5.8%)	7 (5.8%)	1
Acute kidney injury	2 (1.6%)	2 (1.6%)	1
Procedural duration, minutes	36 [25; 50]	56 [49; 77]	<0.0001
Fluoroscopy time, minutes	9 [6;13]	12.7 [8.5; 17]	0.001
Contrast medium, mL	120 [90; 160]	190 [140; 250]	<0.0001
Radiation, cGy/cm²	3985 [2585; 6413]	5648 [3397; 9810]	<0.0001

Average number of OCT runs = 3.8±1.4

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Clinical outcomes at 6 months

Variable	Angio-guided group (n=119*)	OCT-guided group (n=120)	P value
Death from any cause	0	1 (0.8%)	0.32
Myocardial infarction	1 (0.8%)†	1 (0.8%)†	1
Stent thrombosis	0	0	
Target vessel revascularization	1 (0.8%)	2 (1.6%)	0.57
≥1 of the above	**2 (1.6%)**	**3 (2.5%)**	**0.66**

* One pt lost to FUP (death registries indicated the pts was still alive at study cut-off date)
† Both unrelated to target vessel

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Discussion

- The findings of the DOCTORS study suggest that there may be a role for OCT on top of fluoroscopy for the guidance of PCI in ACS.
- Pre-PCI OCT run did not appear to impact on procedural strategy, with the exception of greater use of GP IIb/IIIa inhibitors.
- Conversely, the post-PCI prompted a change in procedural strategy in half of the pts in the OCT-guided group.
- Whether the improvement obtained in FFR will translate into clinical benefit remains to be determined. Nevertheless, the proportion of pts with post-PCI FFR ≥ 0.90 was increased by 22% in the OCT-guided group.
- In view of the study design, it is likely that there is potential to reduce the number of OCT runs and consequently the fluoroscopy time and volume of contrast medium.

Conclusion

- DOCTORS is the 1st RDZ trial to investigate the use of OCT on top of angiographic guidance during PCI in patients with ACS.
- OCT provided useful information beyond that obtained by angiography alone.
- The OCT findings impacted directly on physician decision-making, leading to a change in procedural strategy in half of cases, and was associated with higher FFR at the end of the procedure than PCI guided by fluoroscopy alone.
- This improvement was driven mainly by optimization of stent expansion.
- The benefit was obtained at the cost of a longer procedure with higher fluoroscopy time and more contrast medium, but without an increase in peri-procedural MI or kidney dysfunction.
- Additional prospective studies with clinical endpoints are required before considering incorporating OCT guidance for standard use in patients with ACS.

ORIGINAL RESEARCH ARTICLE

Optical Coherence Tomography to Optimize Results of Percutaneous Coronary Intervention in Patients with Non–ST-Elevation Acute Coronary Syndrome

Results of the Multicenter, Randomized DOCTORS Study (Does Optical Coherence Tomography Optimize Results of Stenting)

Editorial, see p 918

BACKGROUND: No randomized study has investigated the value of optical coherence tomography (OCT) in optimizing the results of percutaneous coronary intervention (PCI) for non–ST-segment elevation acute coronary syndromes.

METHODS: We conducted a multicenter, randomized study involving 240 patients with non–ST-segment elevation acute coronary syndromes to compare OCT-guided PCI (use of OCT pre- and post-PCI; OCT-guided group) to fluoroscopy-guided PCI (angiography-guided group). The primary end point was the functional result of PCI assessed by the measure of post PCI fractional flow reserve. Secondary end points included procedural complications and type 4a periprocedural myocardial infarction. Safety was assessed by the rate of acute kidney injury.

RESULTS: OCT use led to a change in procedural strategy in 50% of the patients in the OCT-guided group. The primary end point was improved in the OCT-guided group, with a significantly higher fractional flow reserve value (0.94±0.04 versus 0.92±0.05, P=0.005) compared with the angiography-

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