Revascularization of Occluded Right Coronary Artery and Outcome After Coronary Artery Bypass Grafting

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Abstract

Objectives The aim of the present study was to evaluate the results of isolated coronary artery bypass grafting (CABG) with or without revascularization of the occluded right coronary artery (RCA).

Methods Patients undergoing isolated CABG were included in a prospective European multicenter registry. Outcomes were adjusted for imbalance in preoperative variables with propensity score matching analysis. Late outcomes were evaluated with Kaplan–Meier's method and competing risk analysis.

Results Out of 2,948 included in this registry, 724 patients had a total occlusion of the RCA and were the subjects of this analysis. Occluded RCA was not revascularized in 251 (34.7%) patients with significant variability between centers. Among 245 propensity score-matched pairs, patients with and without revascularization of occluded RCA had similar early outcomes. The nonrevascularized RCA group had increased rates of 5-year all-cause mortality (17.7 vs. 11.7%, $p = 0.039$) compared with patients who had their RCA revascularized. The rates of myocardial infarction and repeat revascularization were only numerically increased but contributed to a significantly higher rate of MACCE (24.7 vs. 15.7%, $p = 0.020$) at 5 year among patients with nonrevascularized RCA.

Conclusion In this multicenter study, one-third of totally occluded RCAs was not revascularized during isolated CABG for multivessel coronary artery disease. Failure to revascularize an occluded RCA in these patients increased the risk of all-cause mortality and MACCEs at 5 years.

Keywords
- coronary artery bypass grafting
- percutaneous coronary intervention
- myocardial infarction
- repeat revascularization
- right coronary artery
- major cardiac and cerebrovascular events

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Introduction

Coronary artery bypass grafting (CABG) for multivessel coronary artery disease has been shown to be a durable treatment method with better survival compared with percutaneous coronary intervention in several subsets of patients.[1] Although CABG should intuitively pursue complete revascularization to prevent late cardiac events and the need for repeat revascularization, its clinical value is a matter of debate.[2,3] This issue is of relevance in the case of total occlusion of main coronary arteries as these lesions are associated with an increased risk of mortality.[4,5] Still, totally occluded coronary arteries are often not revascularized because of the uncertain benefits of revascularization, the more extensive atherosclerotic lesions, narrowed arterial lumen, and the perceived increased risk of graft failure.[6,7] This is particularly true for totally occluded RCA which is the coronary artery most often not revascularized in case of total occlusion.[8] Råmunddal et al[5] reported that the right coronary artery (RCA) is the most frequent totally occluded coronary artery (prevalence of 42%) and this had a trend toward significantly increased risk of death compared with chronic total occlusion of the left anterior descending artery (hazard ratio = 1.10, 95% CI = 0.99–1.23). Despite this, in the case of totally occluded RCA, cardiac surgeons rely on the validity of established collateral circulation from the left coronary arteries to guarantee the myocardial viability of its territory, although there is indirect evidence that this may not be sufficient to produce durable results.[9,10] In the present study, we aimed to investigate the clinical benefits of surgical revascularization of totally occluded RCA from a multicenter registry.

Materials and Methods

Patient Population and Data Collection

The E-CABG registry included 7,352 consecutive patients who underwent isolated CABG at 16 European centers of cardiac surgery from January 2015 to May 2017. The project is registered in Clinicaltrials.gov (Identifier: NCT02319083). Data on preoperative, operative, and early postoperative variables and outcomes were prospectively collected. Eight of the participating centers (Genoa, Italy; Leicester, UK; Milan, Italy; Naples, Italy; Oulu, Finland; Stockholm, Sweden; Trieste, Italy; Verona, Italy) agreed to collect retrospective data also on late events, and this subset of patients formed the basis of this analysis. For the purposes of the present study, only patients with angiographic findings of total occlusion of the RCA were considered in this analysis. Exclusion criteria were prior cardiac surgery and salvage procedure. Data on patients' preoperative characteristics, operative variables, and early postoperative outcomes were prospectively collected in an Access datasheet with prespecified covariates. Definition criteria for preoperative, operative, and postoperative variables have been previously published.[11] Data on the date of death, myocardial infarction, repeat coronary revascularization, and stroke were collected retrospectively from electronic institutional and national registries as well as by contacting regional hospitals, general practitioners, patients, and their relatives. The Institutional Review Board or Ethical Committee of each participating center approved this study.

Outcomes

The primary outcomes of this study were 5-year all-cause mortality, myocardial infarction, stroke, and repeat coronary revascularization as well as a composite of late major cardiac and cerebrovascular events (MACCEs), that is, all-cause mortality, myocardial infarction, stroke, and repeat coronary. Secondary outcomes were the following adverse events occurred during the index hospitalization: prolonged need of inotropes, use of intra-aortic balloon pump and or extracorporeal membrane oxygenation (excluding patients with preoperative use of these mechanical circulatory support devices), reexploration for bleeding, number of transfused red blood units, reexploration for hemodynamic instability, postoperative percutaneous coronary intervention, deep sternal wound infection, dialysis, stroke, intensive care unit and hospital length of stay, in-hospital mortality, and 30-day mortality. For the present study, myocardial infarction was defined as any myocardial infarction occurring 30 days after the index CABG procedure because the diagnosis of perioperative myocardial infarction might differ between centers. Repeat revascularization and stroke were considered occurring any time after surgery.

Statistical Analysis

The linear-by-linear association test, the Kruskall–Wallis test, the Mann–Whitney test, the chi-squared test, and Fisher's exact test were used for univariate analysis of baseline and operative data. Kaplan–Meier's method and the Cox proportional hazard method were employed to evaluate the impact of revascularization of the occluded RCA on late mortality and MACCEs. Competing risk analysis using the Fine–Gray regression model with all-cause death as a competing event was performed because myocardial infarction, stroke, and repeat coronary revascularization might have been hindered by patient's death. Propensity score matching analysis was performed with revascularization of the RCA as the dependent variable considering the following covariates in the logistic regression model: age, gender, estimated glomerular filtration rate, transient ischemic attack or stroke, extracardiac arteriopathy, diabetes, chronic lung diseases, atrial fibrillation, left ventricular ejection fraction $\leq$50%, emergency procedure, critical preoperative state, number of diseased coronary arteries, and bilateral internal mammary artery grafting. Propensity score matching was performed using a caliper width of 0.2 the standard error of the logit, that is, 0.7. Standardized differences $<$0.10 were considered a nonsignificant imbalance between the baseline and operative covariates. All tests were two-sided, and $p < 0.05$ was set for statistical significance. Statistical analyses were performed using a SPSS v. 25 (IBM Corporation, New York, United States) and Stata v. 15.1 (StataCorp LLC, Texas, United States) statistical software.

Results

Patients' selection of this study is summarized in ►**Fig. 1**. Out of 2,948 patients who have been operated at the participating centers from January 2015 to May 2017, 734 (24.9%) patients had an occluded RCA. The SYNTAX score (data available in 2698 patients) varied significantly between the participating centers (mean SYNTAX scores ranging from 22.3 ± 7.4 to 33.6 ± 5.7, $p < 0.0001$).

Out of 724 patients with occluded RCA who fulfilled the inclusion criteria of this analysis, 478 (66.0%) underwent CABG with revascularization of the totally occluded RCA and 246 (34.0%) did not have this artery revascularized. The rate of revascularization of the totally occluded RCA varied between the participating centers from 41.7 to 97.1% ($p = 0.019$). The mean follow-up of this series was 4.6 ± 1.4 years. We estimated that 37 (5.1%) patients were lost to follow-up as they had a follow-up shorter than 4 years.

In the overall series, several risk factors were well balanced between the RCA revascularized and nonrevascularized RCA study groups as shown by standardized differences < 0.10 (►**Table 1**). In this unmatched series, patients with nonrevascularized RCA had similar 30-day mortality compared to patients who had their occluded RCA revascularized (2.0 vs. 1.0%, $p = 0.498$). However, patients with nonrevascularized RCA had higher rates of postoperative dialysis and stroke as well as a longer stay in the intensive care unit and in the hospital. No significant difference was observed in the other early outcomes. At 5 year, the nonrevascularized RCA group had an increased risk of all-cause mortality (18.1 vs. 11.1%, $p = 0.006$), stroke (5.2 vs. 2.4%, $p = 0.031$), and MACCE (25.6 vs. 16.9%, $p = 0.018$).

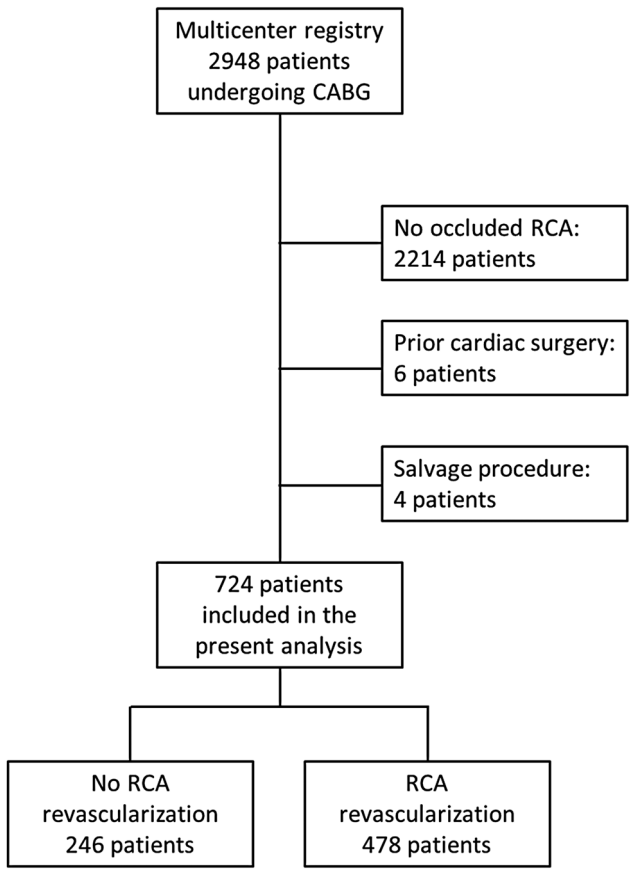

Fig. 1 Flowchart of the study patients' selection. CABG, coronary artery bypass grafting; RCA, right coronary artery.

In the propensity score matched groups, baseline risk factors were well-balanced as shown by standardized differences <0.10. Patients with nonrevascularized RCA had similar 30-day mortality compared to patients who had their totally occluded RCA revascularized (2.0 vs. 1.0%, $p = 0.498$), but their in-hospital stay was longer. No significant difference was observed in other outcomes (►**Fig. 2**). The nonrevascularized RCA group had increased rates of 5-year all-cause mortality (17.7 vs. 11.7%, $p = 0.039$) compared with patients who had their RCA revascularized (►**Table 2**). The rates of myocardial infarction and repeat revascularization were only numerically increased but contributed to a significantly higher rate of MACCE (24.7 vs. 15.7%, $p = 0.020$) at 5 years among patients with nonrevascularized RCA.

Discussion

The main results of the present multicenter study can be summarized as follows: (1) one-third of totally occluded RCA were not revascularized during isolated CABG; (2) the proportion of revascularization varied significantly between centers; (3) failure to revascularize an occluded RCA in patients undergoing isolated CABG for multivessel coronary artery disease increased the risk of all-cause mortality at 5 year; (4) failure to revascularize an occluded RCA during isolated CABG was associated with numerically higher rates of late myocardial infarction and repeat revascularization, which contributed to significantly increased risk of MACCEs at 5 year.

Clinical studies evaluating the prognostic impact of incomplete revascularization provided controversial results[12,13] likely because of the lack of standardization of its definition. Current trials indicate that revascularization was incomplete in one-third of patients undergoing CABG.[12,13] In fact, the SYNTAX study demonstrated that incomplete revascularization does not jeopardize outcomes after CABG at 10 years.[12] However, the definition of incomplete revascularization is not standardized and its value clinical value is vague. In the SYNTAX trial, incomplete revascularization was defined as a failure to revascularize all coronary arteries with ≥50% diameter stenosis in vessels ≥1.5 mm as estimated on the diagnostic angiogram,[12] which translated, in the CABG group, into a proportion of incomplete revascularization of 36.8%. However, the clinical impact of not revascularize a branch of a main coronary artery in an otherwise vascularized myocardial territory may be quite different from a failure to revascularize a diseased main coronary artery. Fefer et al[14] showed that failure to revascularize an occluded coronary artery does not impact patients' survival.

In the multicenter randomized GOPCABE trial,[12] surgical revascularization was defined as complete when the number of performed coronary anastomoses was equal to or higher than the number of anticipated anastomoses. In this trial,

Table 1 Baseline characteristics and operative data in the unmatched and propensity score matched cohorts

Covariates	Unmatched pairs		Matched pairs			
	Revascularized RCA 478 pts	Not revascularized RCA 246 pts	Standardized differences	Revascularized RCA 245 pts	Not revascularized RCA 245 pts	Standardized differences
Baseline risk factors						
Age (years)	66.2 ± 9.0	67.6 ± 8.9	0.149	67.4 ± 8.7	67.5 ± 8.9	0.012
Female	70 (14.6)	39 (15.9)	0.034	43 (17.6)	39 (15.9)	0.044
eGFR (mL/min/1.73 m^2)	78 ± 20	75 ± 23	0.146	74 ± 21	75 ± 23	0.007
Diabetes	153 (32.0)	88 (35.8)	0.080	80 (32.7)	87 (35.5)	0.070
Prior stroke/TIA	42 (8.8)	26 (10.6)	0.060	25 (10.2)	26 (10.6)	0.013
Atrial fibrillation	29 (6.1)	23 (9.3)	0.123	21 (8.6)	23 (9.4)	0.029
Pulmonary disease	56 (11.7)	24 (9.8)	0.063	30 (12.2)	24 (9.8)	0.023
Extracardiac arteriopathy	93 (19.5)	82 (33.3	0.319	87 (35.5)	82 (33.5)	0.043
LVEF ≤ 50%	186 (38.9)	117 (47.6)	0.175	112 (45.7)	116 (47.3)	0.033
Critical preoperative state	45 (9.4)	23 (9.3)	0.002	22 (9.0)	22 (9.0)	0.000
Recent STEMI	43 (9.0)	26 (10.6)	0.053	24 (9.8)	26 (10.6)	0.027
Emergency procedure	19 (4.0)	5 (2.0)	0.113	4 (1.6)	5 (2.0)	0.030
Number of diseased vessels	2.9 ± 0.3	2.9 ± 0.3	0.073	2.9 ± 0.3	2.9 ± 0.3	0.098
SYNTAX score	31 ± 10	33 ± 11	0.177	32 ± 10	33 ± 11	0.106
EuroSCORE II (%)	3.1 ± 4.5	3.5 ± 3.5	0.079	3.6 ± 4.7	3.5 ± 3.5	0.035
Operative data						
Number of distal anastomoses	3.3 ± 0.8	2.2 ± 0.7	1.000	3.3 ± 0.8	2.2 ± 0.7	1.000
CPB time (min)	99 ± 32	74 ± 27	0.838	99 ± 33	74 ± 27	0.810
Aortic clamping time (min)	68 ± 25	47 ± 20	0.869	66 ± 25	48 ± 21	0.806
Off-pump surgery	88 (18.4)	34 (13.8)	0.125	50 (20.4)	34 (13.9)	0.174
BIMA grafting	91 (19.0)	19 (7.7)	0.337	20 (8.2)	19 (7.8)	0.015
Radial artery grafting	23 (4.8)	4 (1.6)	0.181	10 (4.1)	4 (1.6)	0.147
Revascularized RCA branches						
RCA	125 (24.7)	–	–	72 (27.8)	–	–
RPD	216 (42.6)	–	–	103 (39.8)	–	–
RPL	142 (28.0)	–	–	76 (29.3)	–	–
RAM	24 (4.7)	–	–	12 (4.6)	–	–
Multiple distal anastomoses on RCA	27 (5.0)	–	–	14 (5.4)	–	–
RCA endarterectomy	3 (0.6)	–	–	1 (0.4)	–	–
Grafts		–	–		–	–
Vein graft	451 (62.3)	–	–	240 (98.0)	–	–
RIMA graft	22 (3.0)	–	–	4 (1.6)	–	–
Radial artery graft	5 (0.7)	–	–	1 (0.4)	–	–

Abbreviations: BIMA, bilateral internal mammary artery; CAD, coronary artery disease; CPB, cardiopulmonary bypass; eGFR, estimated glomerular filtration rate according to the CKD-EPI equation; EuroSCORE, European System for Cardiac Operative Risk Evaluation; LVEF, left ventricular ejection fraction; PCI, percutaneous coronary intervention; RAM, right acute marginal artery; RCA, right coronary artery; RIMA, right internal mammary artery; RPD, right posterior descending artery; RPL, right posterolateral artery; STEMI, ST-elevation myocardial infarction; TIA, transient ischemic attack.
Note: Clinical variables are according to the EuroSCORE II definition criteria.
Note: Continuous variables are reported as the mean ± standard deviation. Categorical variables are reported as counts and percentages. Anemia is defined as baseline hemoglobin concentration <12.0 g/L in women and <13.0 g/L in men.

incomplete revascularization was associated with a significantly increased risk of mortality at 5 years after either off-pump or on-pump coronary surgery. A few observational studies provided evidence of the beneficial effects of complete surgical revascularization as well.[6,9,15,16] Recently, Fiddicke et al[6] reported the results of a rather small series of patients with chronic totally occluded RCA and they demonstrated that failure to revascularize the RCA was associated with an increased risk of all-cause mortality at 12 years. The study did not report any increased risk of myocardial infarction or repeat revascularization in patients without revascularization of the RCA.

Considering previous studies on the completeness of revascularization as well as the results of studies comparing

Table 2 Crude rates and adjusted risk estimates of outcomes in the unmatched and propensity score matched cohorts

	Unmatched pairs			Matched pairs		
	Revascularized RCA 478 pts	Not revascularized RCA 246 pts	*p*-Value	Revascularized RCA 245 pts	Not revascularized RCA 245 pts	*p*-Value
Early outcomes						
30-d mortality	5 (1.0)	4 (2.0)	0.320	3 (1.2)	5 (2.0)	0.362
In-hospital mortality	5 (1.0)	5 (1.6)	0.498	3 (1.2)	4 (1.6)	0.500
Prolonged need of inotropes	164 (34.3)	78 (31.7)	0.506	88 (35.9)	77 (31.4)	0.170
IABP/ECMO	13 (2.8)	7 (3.2)	0.811	6 (2.5)	7 (3.2)	0.445
Reexploration for bleeding	21 (4.4)	10 (4.1)	1.000	12 (4.9)	10 (4.1)	0.414
Dialysis	7 (1.5)	10 (4.1)	0.037	4 (1.6)	10 (4.1)	0.087
Stroke	0 (0)	3 (1.2)	0.039	0 (0)	3 (1.2)	0.124
ICU stay (days)	2.2 ± 2.2	2.6 ± 2.6	0.050	2.3 ± 2.3	2.6 ± 2.6	0.438
Hospital stay (days)	8.2 ± 6.1	9.3 ± 6.8	<0.0001	8.3 ± 5.9	9.3 ± 6.7	0.002
5-yr outcomes						
All-cause mortality	11.1%	18.1%	0.006	11.7%	17.7%	0.039
Myocardial infarction	3.6%	4.7%	0.671	3.6%	4.3%	0.759
Repeat revascularization	5.9%	6.4%	1.000	3.3%	6.5%	0.254
Stroke	2.4%	5.2%	0.031	4.3%	5.2%	0.478
MACCE	16.9%	25.6%	0.018	15.7%	24.7%	0.020

Abbreviations: ECMO, extracorporeal membrane oxygenation; IABP, intra-aortic balloon pump; MACCE, major adverse cardiac and cardiovascular events; RCA, right coronary artery.
Note: Categorical variables are reported as counts and percentages (in parentheses) and continuous variables as means and standard deviations. Rates of late events are reported as percentages.

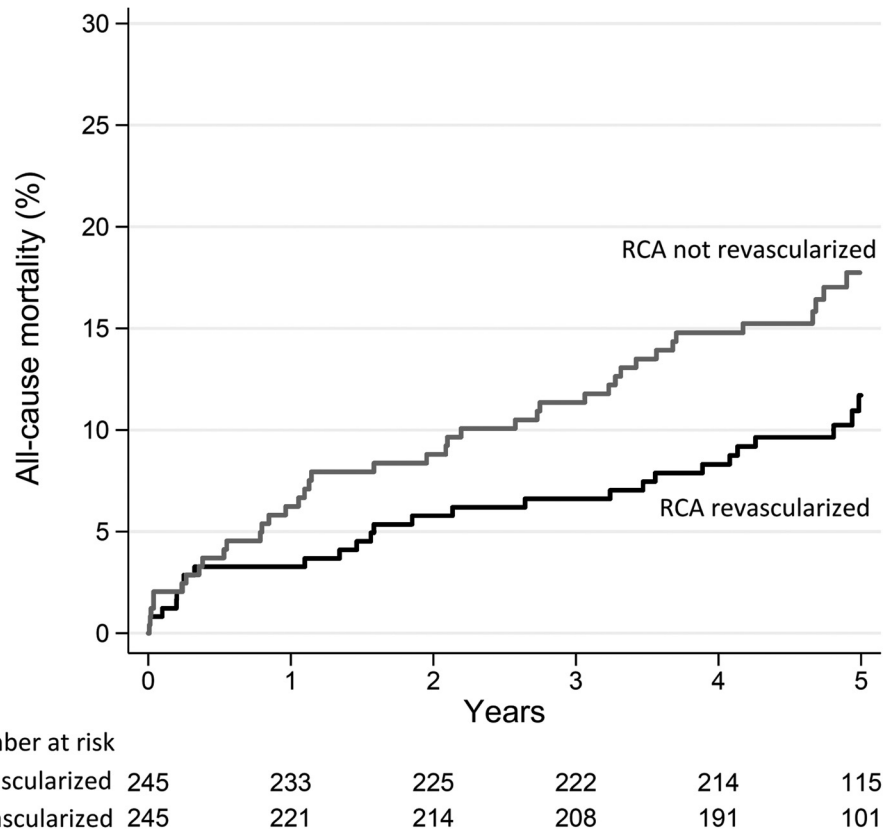

Fig. 2 Kaplan–Meier's estimates of all-cause mortality in propensity score matched patients with and without revascularization of the occluded right coronary artery.

totally occluded RCA compared with medical therapy, the present findings suggest that there may be a benefit in pursuing complete revascularization of totally occluded RCA. Still, we must recognize that in several patients with totally occluded RCA, extensive and calcific atherosclerotic lesions and small caliper of branches with open lumen may still prevent successful and durable revascularization of the RCA territory.[17] The risk of competitive flow from well-developed collateral circulation, instead, should not prevent revascularization of totally occluded coronary arteries.[17]

Several limitations might have affected the validity of the present findings and deserve to be acknowledged. First, although data on baseline, operative, and early postoperative variables were prospectively collected, data on late events were retrospectively collected. Second, we do not have data on myocardium viability, which is an important determinant of outcome, particularly in totally occluded coronary arteries. Third, we do not have data on the feasibility of revascularization to the RCA and its branches. Indeed, we recognize that a review of preoperative angiography might not be useful because the occluded coronary artery is often poorly seen via retrograde filling through collateral circulation.[8] Therefore, in this setting, the feasibility of distal anastomosis can be assessed only during surgery. Fourth, we do not have data on the left and right coronary dominance which might have had anatomic significance in these patients. Finally, retrieval of data on cardiac-related mortality was not feasible in our study.

In conclusion, the results of this study demonstrated that one-third of occluded RCA were not revascularized during isolated CABG for multivessel coronary artery disease. Failure to revascularize an occluded RCA in these patients increased the risk of all-cause mortality and MACCEs at 5 years. Data on potential benefits of surgical revascularization of totally occluded RCA are scarce, and further studies are needed to confirm the present findings.

Ethical Approval for Research

The Institutional Review Board or Ethical Committee of each participating center approved this study.

Authors' Contribution

F.B. was responsible for conceptualization, methodology, and formal analysis; F.B. and Z.E.D. were responsible for software; F.B. and G.M. were responsible for validation; F. B., M.D., T.T., G.G., A.S., F.S., M.D.F., Q.Z, E.M., I.F., C.B., M.Z., T.M., M.S., A.F., F.O., Z.E.D., and G.M. were responsible for investigation and data curation; F.B., M.D., and G.M. were responsible for writing—original draft; F.B., M.D., T.T., G.G., A.S., F.S., M.D.F., Q.Z, E.M., I.F., C.B., M.Z., T.M., M.S., A.F., F.O., Z.E.D., G.M were responsible for writing—review and editing.

Clinical Trial Registration

https://clinicaltrials.gov. Unique identified: NCT02319083.

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Conflict of Interest

None declared.

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