Complete surgical revascularization: different definitions, same impact?

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May 22, 2021

Abstract

Abstract Objectives: There are several different definitions of complete revascularization on coronary surgery across the literature. Despite the importance of this definition there is no agreement on which one has the most impact. The aim of this study was to evaluate which definition of complete surgical revascularization correlates with early and late outcomes. Methods: All consecutive patients submitted to isolated CABG from 2012 to 2016 with previous myocardial scintigraphy were evaluated. Exclusion criteria: emergent procedures and previous cardiac surgery procedures. Population of 162 patients, follow-up complete in 100% patients; median 5,5 IQR 4,4-6,9 years. Each and all of the 162 patients were classified as complying or not with the four different definitions: Numerical, Functional, Anatomical Conditional and Anatomical unconditional. Univariable and multivariable analyses were developed to detect if any definition was a predictor of perioperative and long-term outcomes. Results: Complete functional revascularization was a predictor of increased survival (HR 0.47 CI95: 0,226-0,969; p=0.041). No other definitions showed effect on follow-up mortality. Age and cardiac dysfunction increased long-term mortality. The definition of complete revascularization did not have an impact on MACCE or need for revascularization Conclusions: An uniformly accepted definition of complete coronary revascularization is lacking. This research raises awareness about the importance of viability guidance for CABG.

ORIGINAL ARTICLE

Complete surgical revascularization: different definitions, same impact?

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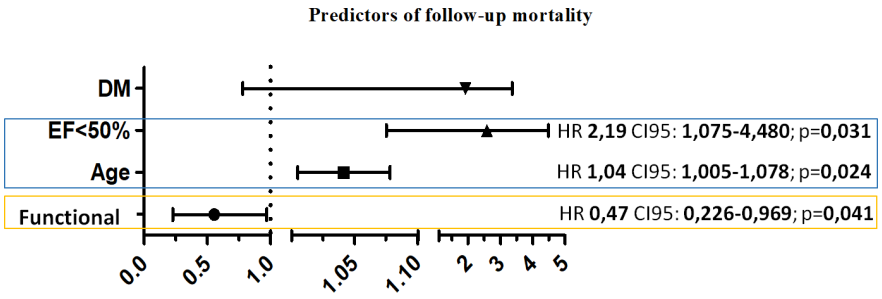
The definition of complete revascularization did not have an impact on MACCE or need for revascularization

Conclusions: An uniformly accepted definition of complete coronary revascularization is lacking. This research raises awareness about the importance of viability guidance for CABG.



Graphical Abstract

KEYWORDS

Coronary disease; complete revascularization; definition; CABG

Key points

Need for a universal definition of complete coronary revascularization.

Complete functional revascularization increases long-term survival in this series.

Abbreviations: CABG, Coronary Artery Bypass Grafting; CPB, cardiopulmonary bypass**;** CR, complete revascularization; DM, Diabetes Mellitus; IQR, interquartile range; LVEF, left ventricle ejection fraction; MACCE, major adverse cardiovascular and cerebrovascular event**;** NYHA, New York Heart Association; PCI, percutaneous coronary intervention**;** RNEC, National Registry for Clinical Studies**;** SD, standard deviation

1| INTRODUTION

Myocardial revascularization is urged to improve symptoms and to provide a better prognosis [1]. The concept of complete revascularization was grounded in early stages [2,3] but recent studies have reported conflicting results [4,5]. Very few clinical studies to date have been conducted to evaluate the impact of complete or incomplete revascularization [2-10]. For this reason, recent guidelines do not undoubtedly support the issue of complete revascularization [1].

One of the reasons that contribute to the wide discrepancies in the reported studies is that there are several different definitions of complete revascularization on coronary surgery across the literature [11]. Despite the importance of this definition there is no agreement on which one has the most impact. We believe that a uniformly accepted definition of complete coronary revascularization is lacking.

The aim of this study was to evaluate which definition of complete surgical revascularization correlates with early and late outcomes.

2| MATERIALS AND METHODS

Between January 2012 and December 2016, a retrospective research identified 1405 patients submitted to isolated coronary artery bypass grafting (CABG) at the Hospital Santa Cruz. Of these patients, 170 underwent assessment of myocardial viability with myocardial perfusion scintigraphy before surgery. Patients with emergency surgery (2) or previous cardiac surgery (6) were excluded. These exclusion criteria were selected *a priori* . Therefore, the study population consisted of **162** patients operated during a 5-year interval.

2.1 | Patient's characteristics

There were 126 men and 36 women (N=162) with median age 66 (IQR 57-75) years. Patient demographics and comorbidities are delineated in Table 1. Twenty-two patients were in NYHA functional class III/IV (13.6%). Reduced left ventricle ejection fraction (LVEF) (<50%) were identified in 42% of the cases. Mean EuroSCORE II of 1.8% (standard deviation (SD): 1.9).

TABLE 1 Patient demographics and comorbidities

Demographics	n (%)
Female sex	36 (22.2)
Mean age (years)	66
NYHA III/IV	22 (13.4)
CCS III/IV	44 (27.2)
LVEF <50%	68 (42)
Mean logistic EuroSCORE II (%)	1.78
Urgency surgery	27 (16.7)
Comorbidities	Comorbidities
Arterial Hypertension	141 (87.0)
DM	79 (48.8)
Dyslipidemia	121 (74.7)
Carotid artery disease	1 (0.6)
Stroke	2 (1.2)
Renal disease	2 (1.2)
Respiratory disease	8 (4.9)
Gastrointestinal disease	5 (3.1)

Abbreviations: CCS, Canadian Cardiovascular Society; DM, Diabetes Mellitus; LVEF, left ventricle ejection fraction; NYHA, New York Heart Association;

2.2 | Operative technique

All procedures were done through a median sternotomy. Standard surgical techniques were used. Heparinization was standardized for off-pump or on-pump surgery. The surgeon was given flexibility and discretion to ensure that his choice of technique would ensure the patient´s safety (including the choice of anatomic regions to revascularize or which graft to use). For the on-pump group, the surgeries were performed with the usual methods of CPB with a single aortic cross-clamp technique. Myocardial protection strategies included antegrade and retrograde blood cardioplegia, and moderate hypothermia. For both types of surgeries, an excellent exposure was required, a motionless and bloodless surgical field and hemodynamic stability of the patient. Conversion from the assigned procedure to the other procedure was performed when clinically necessary. The operative data are listed in Table 2.

TABLE 2 Operative data

Variable	n (%)
On-pump surgery	18 (11.1)
1 Graft	30 (18.5)
2 Grafts	85 (52.5)
3 Grafts	42 (25.9)
4 Grafts	5 (3.1)

2.3 | Definitions of complete revascularization

Based on the paper of Andrew T.L. *et al* [11], each and all the 162 patients were classified as complying or not with the four different definitions: **Numerical:** number of stenotic vessels (a luminal reduction of >_50% in at least one angiographic view) equal to the number of distal anastomoses; **Functional:**all viable myocardial territories are reperfused; **Anatomical Conditional:** all stenotic main-branch vessels (diameter exceeding >_1.5 mm) are revascularized; **Anatomical Unconditional:** all stenotic vessels are revascularized, irrespective of size and territory supplied.

The myocardial viability was assessed with the use of myocardial perfusion scintigraphy. This imaging test was conducted with 99mTc-tetrofosmin and following the stress-rest protocol in use at our hospital. Ultimately, this exam classified the three main myocardial territories as either having or not having myocardial viability.

Each distal anastomosis was counted as a separate graft. Thus, a single sequential conduit counted as more than one graft.

On anatomical definitions, left main trunk stenosis required bypass grafting to both the left anterior descending and left circumflex arteries to achieve complete revascularization.

2.4 | Outcomes and follow-up

Early post-operative outcome was MACCE. Late post-operative outcomes were all-cause mortality and need for revascularization.

MACCE is defined as a composite endpoint including at least one of the following in-hospital variables: in-hospital mortality (mortality of any cause before discharge), myocardial infarction (troponin values > 10 times the 99th percentile of upper reference limit in association with new Q waves), cardiac arrest, stroke and multiple organ failure.

Clinical records and National Data Base were used for long term follow-up. Median follow-up for survival was 5.5 years (IQR: 4.4-6.9) in 100% of patients and freedom from revascularization was 2 years (IQR:1-4) in 91.4%.

2.5 | Statistical Analysis

Categorical variables were expressed as absolute numbers and percentages and continuous variables were expressed as mean (SD) or median (IQR) depending on the distribution. Kolmogorov-Smirnov test was used to access the normal distribution.

The pre-operative variables were selected *a priori* (not a stepwise method): age, gender, hypertension, Diabetes Mellitus (DM), dyslipidemia, New York Heart Association (NYHA) III/IV, Canadian Cardiovascular Society (CCS) scale III/IV, LVEF <50%, renal disease, carotid artery disease, respiratory disease, gastrointestinal disease, urgency surgery and history of stroke. Categorical variables were compared using $\chi 2$ test. Mann–Whitney U-test was used for independent samples not normally distributed.

Variables with a univariate p <0.05 were included in the Multivariable Cox Proportional Hazards Regression and Logistic Regression models to identify risk factors for MACCE and follow-up mortality. A probability

value of p <0.05 was considered statistically significant. All analyses were performed using IBM SPSS Statistics for Windows, Version 22.0. (IBM Corp. Armonk, NY).

3 | RESULTS

3.1 | Completeness of revascularization

Fifty-seven patients (35.2%) were submitted to a complete numerical revascularization. Complete functional revascularization was achieved in 82 patients (50.6%), complete anatomical conditional in 63 patients (38.9%) and 21 patients (13%) were submitted to a complete anatomical unconditional revascularization (Table 3).

3.2 | Early post-operative outcomes

A total of 5 patients (3.1%) died during hospital stay. The mean length of stay was 9.7 (SD:8.4) days. The incidence rate of perioperative MACCE was 9.9%. The detailed list of MACCE is listed in Table 4. On univariable analysis, any of the different definitions of complete revascularization had impact on MACCE. NYHA III/IV (p=0.046) was a significant predictor of MACCE (Table 5).

Table 3: Completeness of revascularization

Type	Complete revascularization (%)
Numerical	35.2
Functional	50.6
Anatomical Conditional	38.9
Anatomical Unconditional	13

TABLE 4 Perioperative MACCE

Morbidity	n (%)
In-hospital mortality	5 (3.1)
Myocardial infarction	5 (3.1)
Cardiac arrest	2 (1.2)
Stroke	1 (0.6)
Multiple organ faillure	2 (1.2)
Total (%)	**9.9**
Mean ventilation time (hours)	11.6
Mean hospital stay (days)	9.7

TABLE 5 Predictors of perioperative MACCE on univariable analysis

Variable	Univariable analysis (p value)
Numerical	0.151
Functional	0.231
Anatomical Conditional	0.243
Anatomical Unconditional	0.133
Female sex	0.088
Mean age	0.599
NYHA III/IV	**0.046**
CCS III/IV	0.319
LVEF <50%	0.335
Arterial Hypertension	0.133

Variable	Univariable analysis (p value)
DM	0.357
Dyslipidemia	0.187
Carotid artery disease	0.901
Stroke	0.812
Renal disease	0.812
Respiratory disease	0.180
Gastrointestinal disease	0.590

Abbreviations: CCS, Canadian Cardiovascular Society; DM, Diabetes Mellitus; LVEF, left ventricle ejection fraction; NYHA, New York Heart Association;

3.2 | Late outcomes

During the follow-up period, thirty-four patients died (21%). As listed in Table 6, complete functional revascularization (p=0.013) was a predictor of increased survival, on univariable analysis. No other definition of complete revascularization showed effect on follow-up mortality. Age (p=0.003), DM (p=0.028) and LVEF <50% (p=0.028) increased the risk of follow-up mortality.

On multivariable analysis, complete functional revascularization (HR 0.47 CI95: 0,226-0,969; p=0.041) was associated with a lower risk of follow-up mortality. Age (HR 1.04 CI95: 1.005-1.078; p=0.024) and EF<50% (HR 2.19 CI95: 1.075-4.480; p=0.031) were independent predictors of increased follow-up mortality (Figure 1).

During the follow-up, twenty-six patients (16%) required repeat surgical or percutaneous revascularization. On univariable analysis, none of the different definitions of complete revascularization had impact on need for repeat revascularization. Dyslipidemia (p=0.016) was a significant predictor (Table 7).

TABLE 6 Predictors of follow-up mortality on univariable analysis

Variable	Univariable analysis (p value)
Numerical	0.281
Functional	**0.013**
Anatomical Conditional	0.069
Anatomical Unconditional	0.538
Female sex	0.500
Mean age	**0.003**
NYHA III/IV	0.299
CCS III/IV	0.287
LVEF <50%	**0.008**
Arterial Hypertension	0.313
DM	**0.028**
Dyslipidemia	0.198
Carotid artery disease	0.790
Stroke	0.623
Renal disease	0.287
Respiratory disease	0.470
Gastrointestinal disease	0.299

Abbreviations: CCS, Canadian Cardiovascular Society; DM, Diabetes Mellitus; LVEF, left ventricle ejection fraction; NYHA, New York Heart Association;

FIGURE 1 Predictors of follow-up mortality on multivariable analysis

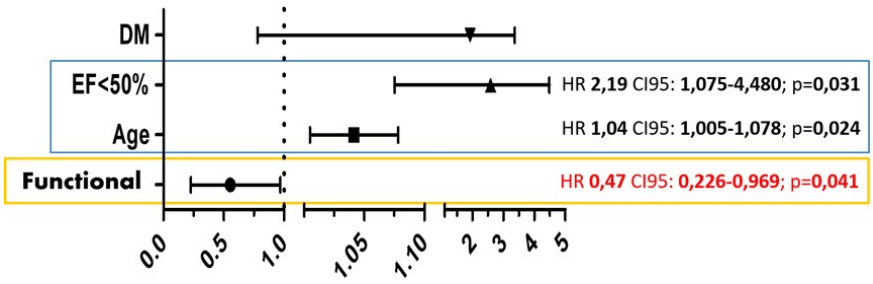


TABLE 7 Predictors of need for revascularization

Variable	Univariable analysis (p value)
Numerical	0.391
Functional	0.389
Anatomical Conditional	0.399
Anatomical Unconditional	0.555
Female sex	0.544
Mean age	0.214
NYHA III/IV	0.271
CCS III/IV	0.241
LVEF <50%	0.432
Arterial Hypertension	0.555
DM	0.530
Dyslipidemia	**0.016**
Carotid artery disease	0.160
Stroke	0.704
Renal disease	0.704
Respiratory disease	0.238
Gastrointestinal disease	0.588

Abbreviations: CCS, Canadian Cardiovascular Society; DM, Diabetes Mellitus; LVEF, left ventricle ejection fraction; NYHA, New York Heart Association;

4 | DISCUSSION

To the best of our acknowledgement, this is the first study that compares different definitions of CR in the same patient, abolishing all confounding variables of multi-person analysis. In this series, a complete functional revascularization (all viable myocardial territories are reperfused) was the only definition with increased long-term survival after coronary surgery. According to recent studies, CR based on the functional definition is the preferred strategy for PCI [1]. However, the role of functional revascularization for CABG is not so obvious [12-14]. For example, the substudy of the STITCH TRIAL failed to prove that a functional revascularization was associated with a greater likelihood of survival in ischemic left ventricular dysfunction, when adjusted for patients' baseline variables [12]. Toth *et al* [13] did not find a significant difference of adverse cardiovascular events at 3 years between patients with fractional flow reserve-guided CABG and angiography-guided CABG.

In literature, there are many different definitions of CR [11]. Probably the most used definition is the anatomical conditional revascularization, where all epicardial vessels with a diameter exceeding [?]1.5 mm

and a luminal reduction of [?]50% in at least one angiographic view are revascularized. Recent studies supported by this definition have reported conflicting results. An example is two different *post hoc* analysis of the SYNTAX trial data, with one study concluding that incomplete surgical revascularization did not impact outcomes, while the other study found relation between incomplete revascularization and adverse outcomes [4,5]. In this study, an incomplete anatomical conditional revascularization was not associated with an increased follow-up mortality.

Complete anatomical unconditional revascularization (all stenotic vessels are revascularized, irrespective of size and territory supplied) is very difficult to achieve as seen in our study with only 13% of the patients. Most common reasons are calcified/diffusely diseased small vessels, difficult exposure, hemodynamic instability, porcelain aorta and limited conduits. Furthermore, this definition has not beeing associated with increased survival in literature [8]. Our research reached the same conclusion. From a survival perspective, the added effort to bypass all branch vessels may not be necessary.

This series validated that numerical revascularization - number of stenotic vessels equals to the number of distal anastomoses - is not relevant in clinical practice.

Our study also verified that age and cardiac dysfunction are independent predictors of late mortality, as seen in earlier studies [3].

There are limited data regarding the relation between CR and perioperative outcomes. Lee *et al* found a relation between incomplete revascularization and MACCE in patients with left ventricular dysfunction [10]. In this research, the definition of complete revascularization did not have an impact on MACCE, possibly indicating the impact of complete revascularization appears to be maximal in the long term.

The need to repeat revascularization was not associated with any definition of CR. A low number of events can explain this result.

This study has multiple limitations. It is based on the retrospective analysis of a population determined by having or not a myocardial perfusion scintigraphy prior to CABG. For that reason, it is a small sample size with low number of events. Surgery was carried by different surgeons and the revascularization was dependent on their clinical assessment. It was not possible to evaluate the reasons for incomplete revascularization. The constrained access to other institutions' records limited us to accurately identify morbidity during follow-up.

5 | CONCLUSION

In summary, a uniformly accepted definition of complete coronary revascularization is lacking in the literature. In this research, a complete functional revascularization was the only definition associated with an increased long-term survival, warning for the importance of viability guidance for CABG.

CONFLICT OF INTEREST

The Authors declare that there is no conflict of interest.

HUMAN ETHICS APPROVAL DECLARATION

The Informed Consent was waived by the Ethics' Committee of our institution (RNEC number 20170700050 at 18th December 2020).

AUTHOR CONTRIBUTIONS

Paulo Veiga Oliveira: Conceptualization; Data curation; Formal Analysis; Investigation; Methodology; Project administration; Software**;** Visualization; Writing – original draft.**Márcio Madeira:** Conceptualization; Data curation; Project administration; Resources; Supervision; Validation; Writing – review & editing. **Sara Ranchordás:** Resources; Supervision; Validation; Writing – review & editing. **Marta Marques:** Resources; Supervision; Validation; Writing – review & editing. **Manuel Almeida:** Supervision; Validation; Writing – review & editing.**Miguel Sousa-Uva:** Resources; Supervision; Validation; Writing – review &

editing. **Miguel Abecasis:** Resources; Supervision; Validation; Writing – review & editing. **José Pedro Neves:**Resources; Supervision; Validation; Writing – review & editing.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request. The data set will be archived for at least 10 years after publication.

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