LISBOA
UNIVERSIDADE DE LISBOA

FACULDADE DE MEDICINA LISBOA

**TRABALHO FINAL**
**MESTRADO INTEGRADO EM MEDICINA**

Clínica Universitária de Cirurgia Vascular

# Synchronous carotid and cardiac surgery: a low risk procedure in high-risk patients

Pedro Miguel Antunes Meireles

**JULHO'2017**

UNIVERSIDADE DE LISBOA

FACULDADE DE MEDICINA LISBOA

**TRABALHO FINAL**
**MESTRADO INTEGRADO EM MEDICINA**

Clínica Universitária de Cirurgia Vascular

# Synchronous carotid and cardiac surgery: a low risk procedure in high-risk patients

Pedro Miguel Antunes Meireles

**Orientado por:**

Professor Doutor Luís Mendes Pedro

**JULHO'2017**

# RESUMO

***Revisão***: As complicações neurológicas são um risco importante da cirurgia cardíaca e o acidente vascular cerebral (AVC) ocorre em cerca de 2% de todos os procedimentos de revascularização do miocárdio. As causas de AVC pós-operatórias são multifactoriais e ainda não é totalmente compreendido o papel da doença carotídea no risco da cirurgia cardíaca. A cirurgia cardíaca e carotídea síncrona é um procedimento realizado em vários centros, em doentes selecionados com múltiplas co-morbilidades. ***Objetivos***: (1) Analisar a segurança da cirurgia síncrona, quando efectuada por uma equipa experiente, em doentes de alto risco cirúrgico; (2) Comparar a mortalidade e risco de AVC entre doentes com diferentes graus de estenose, ou que fizeram cirurgia com circulação extracorporal ou *off-pump*; (3) Avaliar o Euroscore enquanto método estimativo de prognóstico em doentes submetidos a cirurgia cardíaca. ***Métodos***: Um estudo retrospectivo foi conduzido, incluindo dois grupos dum total de 217 doentes submetidos a cirurgia carotídea e cardíaca síncrona, entre os anos 2000-2017 no Hospital de Santa Maria, em Lisboa. A análise estatística foi realizada com recurso a *Fisher test* ou teste do qui-quadrado e *Mann-whitney test*. ***Resultados***: No total, apenas 1 doente (0.46%) teve um AVC ipsilateral 24 horas após a cirurgia. Quatro doentes (1.84%) sofreram um AVC isquémico ou hemorrágico no hemisfério contralateral ou no cerebelo, sendo a taxa de mortalidade global de 7.83%. Não foi registada uma diferença estatisticamente significativa na taxa de mortalidade (p=0.524) entre doentes com diferentes graus de estenose. Não foi registada uma diferença estatisticamente significativa na taxa de mortalidade (p=0.521) entre os doentes que fizeram cirurgia com circulação extracorporal ou off-pump. Constatou-se um aumento estatisticamente significativo na mortalidade (p=0.0041) e no risco de complicações major (p=0.0006) com o aumento do Euroscore. ***Conclusões***: A cirurgia síncrona, efectuada por uma equipa experiente, tem um risco neurológico baixo, mesmo em doentes *Euroscores* elevados. A extensão da doença carotídea entre os grupos estudados não teve influência no resultado cirúrgico.

**Palavras-chave**: AVC, Estenose carotídea, Cirurgia cardíaca, Cirurgia síncrona.

Este Trabalho Final exprime a opinião do autor e não da FML.

# ABSTRACT

***Background***: Neurologic complications remain an important risk of cardiac surgery, as stroke occurs in about 2% of all myocardial revascularization procedures. The causes of post-CABG stroke are multifactorial and it is not fully understood whether the presence of concomitant severe carotid disease increases the risk of the cardiac procedure. Several strategies have been attempted, and the synchronous carotid and cardiac surgery is a procedure that is frequently performed worldwide in patients with multiple co-morbidities. ***Objectives***: (1) To analyse the safety of the synchronous surgery, when performed by an experienced team, in high-risk patients; (2) To compare the mortality and the risk of stroke between patients with different degrees of stenosis or undergoing on surgery with extracorporeal circulation and off-pump; (3) To evaluate the Euroscore as a tool to establish the prognosis of patients undergoing cardiac surgery. ***Methods***: A retrospective study was conducted, including two groups of a total of 217 patients, with different degrees of stenosis, undergoing synchronous cardiac and carotid surgery, between the years 2000-2017 in Hospital Santa Maria, Lisbon. The statistical analysis was performed using a *Fisher test* or a $\chi^2$ test and a *Mann-whitney test*. ***Results***: Overall, only 1 patient (0.46%) has suffered an ipsilateral stroke 24 hours after the procedure. Four patients (1.84%) had suffered an ischemic or haemorrhagic stroke on the contralateral hemisphere or on the cerebellum and the global mortality rate was 7.83%. We have not registered a significant difference in the mortality rates (p=0.524) between patients with different degrees of stenosis. There is no significant difference in the mortality rates (p=0.521) in patients undergoing surgery with extracorporeal circulation and off-pump. There is an increasing risk of death (p=0.0041) and risk of major complications (p=0.0006) in patients with higher Euroscores. ***Conclusions***: The synchronous surgery, performed by an experienced team, has a very low neurological risk, even in patients with high Euroscore levels and significant co-morbidities. The extension of the carotid disease among the groups we have studied did not have different significant outcomes.

**Key Words**: Stroke, Carotid stenosis, Cardiac surgery, Synchronous surgery

This Final Paper expresses the author's opinion and not the FML's.

# ÍNDICE DE TABELAS

# ÍNDICE

## INTRODUCTION

Neurologic complications remain an important risk of cardiac surgery and the several strategies that were introduced to reduce its incidence were not fully effective. The incidence of stroke after coronary artery bypass grafting (CABG) surgery is around 2% but it rises to 5-8% when valvular replacement is added [(1)]. Interestingly, most strokes after cardiac surgery are delayed and 62% were found to appear more than 24 hours after the procedure. The causes of post-CABG stroke are multifactorial and, since the typical patient has advanced atherosclerotic disease, some of them will also present with severe carotid disease. Approximately 17% of patients undergoing myocardial revascularization are noted to have moderate to severe carotid artery stenosis [(2)] (CAS), while 28% have significant coronary artery disease and may be candidates for carotid endarterectomy (CEA)[(3)]. The optimal management of the patients requiring cardiac surgery with concomitant severe carotid disease remains a controversy.

A significant number of systematic reviews [(4, 5, 6, 7, 8, 9)] have previously concluded that carotid disease is an important cause of stroke after cardiac surgery and they were unanimous in developing an evidence-based strategy for recommending prophylactic or combined CEA/CABG. However, evidence suggests that much of the data supporting a role for prophylactic intervention may be open to debate. It is still a matter of discussion, for instance, whether these outcomes are centred in symptomatic patients or are also seen in asymptomatic cases, and enough data is not available for conclusions at this moment.

The purpose of this study is to evaluate and share the experience of a working group of a tertiary centre in the treatment of a group of patients, with concomitant cardiac and carotid disease, undergoing synchronous carotid and cardiac surgery. We compared the outcomes for patients who were symptomatic and asymptomatic, and had different degrees of stenosis. We intend to provide as much information as possible regarding the patients' outcomes and to compare their mortality and neurological morbidity rates to the data published in the literature, demonstrating that this is a low-risk procedure in patients with advanced co-morbidities. We have used the Euroscore to evaluate the cardiac pre-operative risk in all patients.

## MATERIAL AND METHODS

### Patient Population

Since the year 2000, asymptomatic and symptomatic patients, who underwent on cardiac surgery and had an underlying severe carotid disease, were scheduled to have synchronous cardiac and carotid surgery at Hospital Santa Maria, Lisbon. We have retrieved the patients' indication for cardiac surgery, their demographic data, risk factors for atherosclerosis, Euroscore, degree of stenosis and the use of extracorporeal circulation from our vascular registry, from our vascular registry.

For purposes of definition, multi-organ failure, pneumonia, renal failure, perioperative bleeding, cervical haematoma, acute myocardial infarction, cardiogenic shock, mediastinitis and stroke, which involved hospitalization for more than five days in the Intensive Care Unit (ICU), were all regarded as major complications. Patients with previous history of stroke, amaurosis fugax or transient ischemic accident were regarded as symptomatic patients.

In order to investigate the role of carotid disease in the surgical outcomes, we have analysed the risk of death and the risk of stroke and divided the patients into two groups: Group 1 – patients with ipsilateral internal carotid artery stenosis >70% and contralateral internal carotid artery stenosis <70%; Group 2 – patients with bilateral internal carotid artery stenosis >70% or ipsilateral stenosis >70% and contralateral occlusion. The degree of stenosis was calculated using eco-doppler imaging by experienced vascular surgeons and technicians from the vascular and neurology's laboratory.

The population in this study includes a total of 217 patients submitted to synchronous carotid and cardiac surgery. One hundred and fifty-four (71%) are male and sixty-three (29%) are female and their mean±SD age is 70.91±10.39 years (52-85). The patients have a median Euroscore level of 11.42, which made them accessed as "high-risk patients".

All patients were operated on the Cardiothoracic Surgery Operating Room in Hospital Santa Maria, Lisbon, from 2000 to 2017.

**Cerebrovascular Disease and Carotid Surgery**

One hundred and eighty-six (85.7%) patients did not have any previous neurological symptom and thirty-one (14.3%) were symptomatic, with previous history of stroke (23), transient ischemic attack (7) or *amaurosis fugax* (1) over the past 6 months.

All patients undergoing carotid surgery had carotid stenosis over 70%. The median range of stenosis in the operated carotid artery was 90% (70-95%) (see Table 1). The contralateral internal carotid artery presented a median stenosis degree of 50%. Thirteen patients (6%) had a complete occlusion of the contralateral internal carotid artery, forty-four cases (20.3%) had 70-99% stenosis and ninety-seven patients (44.7%) had 50-69%. In sixty-three patients (29%), the contralateral stenosis was <50%.

According to this data, the vascular procedure was indicated by unilateral stenosis >70% in one hundred and twenty-four (57.1%) patients, by unilateral stenosis >70% associated with contralateral stenosis 60-69% in thirty-six (16.6%) patients, by bilateral stenosis >70% in forty-four (20.3%) patients and finally by unilateral stenosis >70% associated with contralateral occlusion in thirteen (6%) patients (see Table 1).

The carotid procedure was performed immediately before the sternotomy and always by the same vascular surgeon (LMP). The carotid procedure included two-hundred and four (94%) cases of conventional endarterectomy (CEA), nine (4%) cases of eversion CEA, two (1%) cases of venous interposition between the common carotid artery and the internal carotid artery and two (1%) cases of ascending aorta to carotid bifurcation or innominate artery bypass. The CEA was closed with patch (venous in two-hundred cases – 98%, and Dacron in four cases – 2%). Anticoagulation with non-fractioned heparin IV in a dose of 2000-2500 units was always administered before carotid clamping. A shunt during the carotid clamping period was inserted according to the residual pressure criteria (shunt if residual pressure < 50 mmHg). Shunting was used in seventy-five (34.6%) cases (Pruitt-Inahara in 70 and Javid in 5).

The cervical incision was always closed at the end of the carotid procedure in all but one case, where the haemostasis was inadequate and the neck was closed after the cardiac surgery.

## Cardiac Surgery

Cardiac procedure: The cardiac surgery was performed by isolated valvular disease, isolated severe coronary disease or combined with valvulopaty, left-ventricular aneurism or auricular mixoma. CABG, single or multiple, was performed in one-hundred and thirty-nine cases (64.1%), CABG associated with valvular replacement in forty-six cases (21.2%), CABG associated with pericardiectomy in one case (0.5%), CABG associated with ventricular aneurismectomy in one case (0.5%), CABG associated with a pacemaker implantation in one case (0.5%) and CABG associated with a mixoma resection in one case (0.5%). In twenty-six cases (12%), isolated valvular replacement was performed. Extra-corporeal circulation was used in sixty-nine cases (31.8%), while in one-hundred and forty-eight cases (68.2%) the surgery was performed off-pump (see Table 1).

## Statistical Analysis

Continuous variables were expressed as mean±SD if symmetrically distributed and comparison was made by t-student test. Asymmetrical distribution continuous data were expressed as median (range) and compared with Mann-Whitney test. Categorical data were summarized as frequencies and percentages and compared using the Fisher exact test. Multivariate logistic regression analysis was performed to control for confounders.

All statistical analysis was conducted using Stata 12.1 software (Stata Corporation, College Station, TX).

**Table 1**: Demographic data.

| | n | % |
|---|---|---|
| **All patients** | **217** | |
| Male | 154 | 71 |
| Female | 63 | 29 |
| | | |
| **Symptoms** | | |
| Symptomatic | 31 | 14.3 |
| - *Stroke* | *23* | |
| - *TIA* | *7* | |
| - *Amaurosis fugax* | *1* | |
| Asymptomatic | 186 | 85.7 |
| | | |
| **Carotid disease:** | | |
| HOMOLATERAL | | |
| 70-79% | 16 | 7.4 |
| 80-89% | 85 | 39.2 |
| 90-99% | 116 | 53.4 |
| CONTRALATERAL | | |
| <50% | 63 | 29 |
| 50-59% | 61 | 28.1 |
| 60-69% | 36 | 16.6 |
| 70-79% | 21 | 9.7 |
| 80-89% | 15 | 6.9 |
| 90-99% | 8 | 3.7 |
| Occlusion | 13 | 6 |
| | | |
| Unilateral >70% | 124 | 57.1 |
| Unilateral >70% + Controlateral 60-69% | 36 | 16.6 |
| Bilateral >70% | 44 | 20.3 |
| Unilateral >70% + Controlateral occlusion | 13 | 6 |
| | | |
| **Cardiac procedure:** | | |
| CABG | 139 | 64.1 |
| CABG+pericardiectomy | 1 | 0.46 |
| CABG+ valvular replacement | 46 | 21.2 |
| CABG+ventricular aneurysmectomy | 1 | 0.46 |
| CABG+pacemaker | 1 | 0.46 |
| CABG+Mixoma resection | 1 | 0.46 |
| Isolated valvular replacement | 26 | 12 |
| Unkown | 2 | 0.92 |
| | | |
| CBP | 69 | 31.8 |
| Off Pump | 148 | 68.2 |

## RESULTS

Table 2 presents the results of this series 30 days after the procedure.

Overall, of the total 217 patients, none of the patients had an intra-operatory stroke. However, one patient (0.46%) has suffered an ipsilateral stroke 24 hours after the procedure. Four patients (1.84%) had suffered an ischemic or haemorrhagic stroke on the contralateral hemisphere or on the cerebellum (see Table 2). The overall mortality rate was 7.83% (17 deaths).

We registered thirteen deaths (8.1%) from Group 1 and four deaths (7%) from Group 2. One patient (1.75%) from Group 2 suffered an ipsilateral stroke 24 hours after the procedure. Two patients (1.3%) from Group 1 and two patients (3.5%) from Group 2 suffered an ischemic or haemorrhagic stroke on the contralateral hemisphere or on the cerebellum, and all of them have died.

The overall mortality rates between the two groups was not significantly different (p=0.524), neither was the risk of any stroke (p=0.282). Group 1 had 14.0% (eight patients) of major complications and group 2 had 21.3% (thirty-four patients), with no significant difference between the two groups (p=0.161).

A slightly lower mortality rate, still not statistically significant (p=0.521), was observed when using extracorporeal circulation (7.2% *versus* 8.1%)

## EUROSCORE

Median Euroscore was higher among the patients who died (12.74) than the patients who survived (8.21) (p=0.0041). Patients who have suffered post-operative major complications had a higher Euroscore median value (11.49 *versus* 7.86, p=0.0006).

**Table 2**: 30-day outcomes.

| | n | 30-day Mortality | Ipsilateral stroke | Any stroke | Death + Ipsilateral stroke | Death + Any stroke |
|---|---|---|---|---|---|---|
| | | n (%) | n (%) | n (%) | n (%) | n (%) |
| **All patients** | **217** | **17 (7.83)** | **1 (0.46)** | **4 (1.84)** | **17 (7.83)** | **17 (7.83)** |
| Male | 154 | 10 (6.5) | 1 (0.65) | 4 (2.6) | 10 (6.5) | 10 (6.5) |
| Female | 63 | 7 (11,1) | 0 | 0 | 7 (11,1) | 7 (11,1) |
| Symptomatic | 31 | 3 (9.7) | 1 (3.2) | 2 (6.4) | 3 (9.7) | 3 (9.7) |
| Asymptomatic | 186 | 14 (7.5) | 0 | 2 (1.1) | 14 (7.5) | 14 (7.5) |
| **Carotid disease:** | | | | | | |
| **Group 1** (Ipsilateral >70% + Contralateral <70%) | 160 | 13 (8.1%) | 0 | 2 (1.3%) | 13 (8.1%) | 13 (8.1%) |
| **Group 2** (Bilateral >70% or Ipsilateral >70% + Contralateral occlusion) | 57 | 4 (7%) | 1 (1.75%) | 2 (3.5%) | 4 (7%) | 4 (7%) |
| **Cardiac procedure:** | | | | | | |
| CABG | 139 | 14 (10.1) | 1 (0.7) | 4 (2.9) | 14 (10.1) | 14 (10.1) |
| CABG + pericardiectomy | 1 | 0 | 0 | 0 | 0 | 0 |
| CABG + ventricular aneurysmectomy | 1 | 0 | 0 | 0 | 0 | 0 |
| CABG + pacemaker | 1 | 1 (100) | 0 | 0 | 1 (100) | 1 (100) |
| CABG + mixoma resection | 1 | 0 | 0 | 0 | 0 | 0 |
| CABG + valvular replacement | 46 | 1 (2.2) | 0 | 0 | 1 (2.2) | 1 (2.2) |
| Isolated valvular replacement | 26 | 1 (3.8) | 0 | 0 | 1 (3.8) | 1 (3.8) |
| Unknown | 2 | 0 | 0 | 0 | 0 | 0 |
| CBP | 69 | 5 (7.2) | 0 | 1 (1.4) | 5 (7.2) | 5 (7.2) |
| Off Pump | 148 | 12 (8.1) | 1 (0.7) | 3 (2) | 12 (8.1) | 12 (8.1) |

## DISCUSSION

Stroke remains a serious complication of cardiac surgery and it occurs in about 2% of all myocardial revascularization procedures. It is not yet clear whether the presence of significant carotid disease is an important incremental risk factor for the development of stroke after CABG. A recent updated systematic review and meta-analysis has reported outcomes in patients with severe CAS (70–99% stenosis) or occlusion, undergoing an isolated cardiac procedure, and the prevalence of stroke, death and death/stroke was 7.4%, 4.8% and 6.5%, respectively [10]. Several studies have shown that carotid disease is an important aetiological factor in the pathophysiology of post-CABG stroke [11], considering that the presence of an unilateral carotid stenosis >50% raises the neurological risk to 3%, the presence of bilateral stenosis >50% raises the risk to 5% and when there is contralateral occlusion of the internal carotid artery, the risk of an intra-operative stroke is about 7-11% [12, 13]. These data suggest that the treatment of an underlying carotid lesion might help to reduce the incidence of stroke, which lead to the introduction of several therapeutic strategies, such as a staged CEA followed by cardiac surgery or, more recently, at the same operating time – the synchronous surgery. Furthermore, in the general CABG population, the prevalence of significant CAS is relatively high. The reported prevalence of moderate CAS (more than 50% stenosis) is around 22% [14], which results in a 3.8% stroke rate [15], and the prevalence of severe CAS (more than 80% stenosis) is around 8.5% [14], resulting in a 14% stroke rate [16]. Additionally, the risk of perioperative stroke in CABG patients who reported a prior TIA or stroke has been associated with a fourfold increased risk as compared to the risk for asymptomatic patients [17]. However, most of these studies did not determine whether overall cardiovascular risk of death, stroke or myocardial infarction – usually estimated by the Euroscore – are increased in patients with severe carotid and coronary disease undergoing CABG. On the other hand, there are studies suggesting that there is no direct causal relationship linking postoperative stroke and severe carotid stenosis. Some authors claim that there is a failure to establish a connection between the strokes and the diseased carotid territories raising the hypothesis that these postoperative strokes may be attributable to alternate causes [18]. In a retrospective analysis of 878 patients who underwent on isolated CABG, there was no significant difference in the mortality rates and in the neurological outcomes between patients with severe CAS (defined in this study as >75% stenosis) and patients without severe CAS [20]. A retrospective review by Adams et al. identified 1,499 patients who underwent cardiac

surgical procedures between July 1999 and September 2010 and concluded that most perioperative strokes after cardiac surgery procedures do not arise from carotid lesions but are more likely caused by atheroemboli from arch manipulation, global hypoperfusion associated with low cardiac output, or other causes. They have established that universal carotid artery screening in cardiac surgery patients has not led to a decreased incidence of strokes in the patient population and only few strokes can be directly linked to carotid lesions [21]. In a smaller study of 139 patients with severe (>75% stenosis), unilateral, asymptomatic CAS undergoing CABG, with a group of 73 patients having no carotid artery surgery and a group of 66 patients having staged CEA, Gaudino et al [22] reported no differences between the in-hospital rates of stroke (0% versus 0%; $P$=1.0) or mortality (1.4% versus 1.5%; $P$>0.05). In a series of 50 patients with asymptomatic CAS >70% undergoing CABG without prophylactic CEA, Ghosh et al [23] demonstrated no adverse cerebrovascular incident within 30 days postoperatively, and only 1 experienced a transient ischemia attack at 14 months. Overall, this data represents only a fraction of data compared to the vast amount of previous information demonstrating a high stroke incidence (9.2–11.5%) in isolated CABG, and also describe different patient populations (off or on-pump bypass surgery, asymptomatic or symptomatic patients) [24].

The 2014 European Society of Cardiology's guidelines for myocardial revascularization state that the prevalence of severe carotid artery stenosis increases with the severity of coronary artery disease and is an indicator of impaired prognosis. As so, in patients with previous TIA or stroke and the presence of carotid artery stenosis (50–99% in men; 70–99% in women), CEA performed by experienced teams may reduce the risk of perioperative stroke or death. Carotid revascularization may be considered in asymptomatic men with bilateral severe carotid artery stenosis or contralateral occlusion, provided that the risk of stroke or death within 30 days can be reliably documented to be <3% in the presence of a life expectancy >5 years. In women with asymptomatic carotid disease or patients with a life expectancy of <5 years, the benefit of carotid revascularization remains unclear. Conversely, isolated myocardial revascularization should be performed among patients with asymptomatic unilateral carotid artery stenosis because of the small risk reduction in stroke and death achieved by concomitant carotid revascularization (1% per year) [25, 26].

In our study, we have tested two different groups of patients and we did not find a

statistical significant difference between the group of patients with ipsilateral severe CAS (>70%) and contralateral CAS <70% (Group 1) and patients with bilateral severe CAS (>70%) or ipsilateral severe CAS and contralateral occlusion. The mortality and morbidity rates on both groups were low and agreed to previous studies (8.1% deaths + stokes on Group 1 vs 7% deaths + strokes on Group 2, p=0.524). The risk of any stroke was also low and not statistically different on both groups (1.3% in Group 1 and 3.5% in Group 2, p=0.282).

The incidence of stroke may also be related to the cardiopulmonary bypass, and whether off-pump CABG reduces the evidence of stroke remains controversial. Two large meta-analysis agreed that the benefit of off-pump coronary artery bypass surgery in reducing the incidence of stroke is marginal [27, 28], however, according to a retrospective study of 16.184 patients, the incidence of stroke is shown to be significantly lower with off-pump CABG (2.5%) than with conventional CABG (3.9%) [29]. More recently, Lamy et al. concluded that at 1 year, in a group of 4752 patients scheduled to undergo CABG, there was no significant difference in the rate of the primary composite outcome between off-pump and on-pump CABG (12.1% and 13.3%, respectively), the rate of repeat coronary revascularization, quality of life, or neurocognitive function [30]. Our study shows that the mortality rate on patients undergoing conventional and off-pump CABG has no statistical difference (7.2% and 8.1%, p=0.521, respectively), even when controlled with Euroscore (p=0.409), which correlates with recent data.

Recent randomized controlled trials have attested the safety and efficacy of the synchronous carotid and cardiac procedure in patients with severe CAS with concomitant coronary disease [31, 32]. In a retrospective study with 3700 patients, on which 47 patients were taken for simultaneous CEA and CABG and none of them has suffered from ischemic stroke, myocardial infarction or death during the perioperative period, the synchronous procedure was considered to be safe and effective. Other systematic reviews and meta-analysis, and our own experience, all favour combined surgery as a safe option in cases of severe CAS undergoing CABG [11, 33, 34]. Recent studies have suggested comparable outcomes in the staged and combined approach, without any advantages of one technique over the other, and concluded that patient specific risk factors and morphology of the atherosclerotic disease might be more important determinants of postoperative morbidity and mortality rather than the therapeutic strategy [35]. Recent data states that, although patients undergoing combined

CEA and CABG had higher preoperative risk factors, the combined approach was performed with comparable rates of mortality and major cardiovascular morbidity in the early postoperative period [36].

Our study demonstrates that the synchronous CEA and CABG is a safe procedure, with favorable outcomes, and that does not sustain a higher perioperative mortality rate. We have performed this procedure in a group of 217 patients, throughout the past seventeen years with the same vascular team, and our strategy was associated to a very low risk of ipsilateral perioperative stroke (1 patient, 0.46%) and a very low risk of perioperative stroke overall (4 patients, 1.84%). Our mortality rate was 7.83% (17 patients), but most of all deaths were related to other comorbidities of the patient. CEA seemed to contribute to decrease the rate of ipsilateral stroke to residual levels. However, as expected, it had no impact in contralateral and vertebrobasilar stroke and consequently in the overall stroke risk.

Overall, the patients included in our study we high risk and had a mean Euroscore level of 11.42, and the patients who have died have a mean Euroscore level of 12.74. There is a significant difference (p=0.0041) in the Euroscore level between the patients who have died and those who have survived and between the patients who suffered major complications and those without surgical complications (p=0.001). This means that, as a group, patients with carotid stenosis suffer from other comorbidities that influence the high Euroscore observed and also that mortality seems to be related to the associated diseases and the general medical frailty. This is in consonance to the publications that demonstrate a higher atherosclerotic burden in patients with cerebrovascular disease [21, 32, 37, 38].

**Limitations:** We encountered some limitations in the data collected for this study, which reflect both record keeping by clinicians as well as the current state of the medical record system. First, a few operative notes lacked details concerning the extent and location of coronary and carotid artery disease. Second, since this was a retrospective study, some data was not clear in older folders, which made our evaluation harder and it was not possible to add all the variables we wanted to study since we have lost contact to most of the oldest patients and did not have their discharged papers or information about subsequent consults. Third, patients often did not have a detailed neurological evaluation, which might have provided further understanding of both their

symptoms and extent of nervous system involvement. Fourth, radiological reports often did not describe in sufficient detail the involved cerebral circulation, which might account for a portion of the unclassified strokes. Fifth, we did not have a control group, which made it harder to define our variables.

Despite these limitations, we are confident that our findings are in agreement with the peer-reviewed literature. We have no reason to believe that these limitations severely hampered our ability to make our conclusions.

In conclusion, our study showed that the synchronous surgery, performed by an experienced team, did not incur excess risks, compared with staged interventions. The degree of stenosis seems not having an impact in the risk of stroke or death. However, the Euroscore is related to the overall risk of death in this group of patients and it is safe to assume that patients with higher risk factors for cardiac surgery (higher Euroscore) will be on higher risk of mortality and post-operative complications, irrespectively of being submitted to concomitant carotid revascularization, which seemed to had a positive impact in the prevention of ipsilateral stroke.

Further studies are needed in order to unequivocally prove that CEA does not add benefit to patients undergoing coronary revascularization.

# RESUMO

Os desfechos neurológicos mantêm-se como um comum factor de complicação Da cirurgia cardíaca e as diversas tentativas de diminuir a sua incidência não foram totalmente eficazes. Os principais factores de risco são cardioembólicos, ateroembólicos, hemodinâmicos, e hemorrágicos.

A incidência de Acidente Vascular Cerebral (AVC) após Cirurgia de Revascularização do Miocárdio (CRM) é cerca de 2% e aumenta para 5-8% quando é acrescentado um procedimento de substituição de válvula. Cerca de 17% dos doentes que fazem CRM têm doença carotídea moderada a grave, sendo que 28% são candidatos a endarterectomia. A presença de estenose carotídea unilateral >50% aumenta o risco de complicações neurológicas para 3%, a presença de estenose carotídea bilateral >50% para 5% e a oclusão contralateral da artéria carótida interna para um risco de AVC intra-operatório de 7-11%, o que sugere que a presença de doença carotídea e a sua gravidade são determinantes do risco de complicações neurológicas associadas à cirurgia cardíaca. O melhor método para tratar doentes candidatos a cirurgia cardíaca com doença carotídea grave concomitante mantém-se incerto e gera controvérsia.

A cirurgia carotídea e cardíaca síncrona é um procedimento extensamente utilizado e estudado em vários centros mundiais e pode diminuir o risco e a incidência de complicações neurológicas em doentes com múltiplas co-morbilidades que são submetidos a cirurgia cardíaca. O objectivo desta investigação é analisar o risco-benefício da utilização desta cirurgia em doentes de alto risco cirúrgico e apresentar a experiência do Hospital de Santa Maria durante os anos de 2000-2017, onde mais de 217 doentes foram operados.

A população em estudo engloba 217 doentes, 71% do sexo masculino e 29% do sexo feminino, com uma idade média de 70.91 anos e um *Euroscore* médio de 11.42. 14.3% dos doentes tinham antecedentes pessoais de AVC, Acidente Isquémico Transitório (AIT) ou Amaurose Fugaz, sendo classificados como “sintomáticos”, enquanto que 85.7% eram assintomáticos. No sentido de estudar o papel da doença carotídea nos resultados cirúrgicos, analisou-se o risco de AVC e morte dividindo a população em 2 grupos: Grupo 1- doentes com estenose carotídea unilateral >70% e contralateral <70%, e Grupo 2- doentes com estenose carotídea bilateral >70% ou com estenose unilateral >70% e oclusão contralateral. Todos os doentes submetidos a endarterectomia

convencional (CEA) tinham um grau de estenose superior a 70%. A CEA foi realizada em 94% dos casos, em 4% dos casos foi realizada CEA de eversão, em 1% interposição venosa entre a artéria carótida interna e a artéria carótida comum e em 1% interposição venosa entre a aorta ascendente e a bifurcação carotídea. A CEA foi fechada com patch venoso em 98% dos casos. Foi usada uma dose de Heparina Não-Fraccionada endovenosa (2000-2500UI) antes da clampagem da carótida. Foi realizado shunt durante a clampagem da carótida sempre que a pressão residual era <50mmHg. A incisão cervical foi encerrada em todos os casos após o final do procedimento carotídeo, excepto num caso em que as condições de hemostase não era adequadas. A cirurgia cardíaca foi realizada por doença valvular isolada, doença coronária isolada ou combinada com valvulopatia, aneurisma ventricular esquerdo ou mixoma auricular. Foi realizada circulação extra-corporal em 31.8% dos casos e a cirurgia foi realizada *off-pump* em 68.2% dos casos. A tabela 1 apresenta todos os dados demográficos da população em estudo.

Relativamente aos resultados obtidos, de realçar que não ocorreu nenhuma morte peri-operatória, houve apenas 1 AVC ipsilateral após 24 horas da cirurgia e, no total, morreram 4 doentes com AVC isquémico ou hemorrágico no hemisfério contralateral ou no cerebelo. A taxa de mortalidade global foi de 7.83%. Em relação aos doentes do grupo 1, houve uma taxa de mortalidade de 8.1%, dos quais 1 AVC cerebelar e 1 AVC do hemisfério contralateral, enquanto que no grupo 2 a taxa de mortalidade foi 7%, tendo ocorrido 1 AVC ipsilateral e 1 AVC do hemisfério contralateral. A mortalidade foi ligeiramente inferior nos doentes com circulação extra-corporal, embora não estatisticamente significativa (p=0.521). O Euroscore médio entre os doentes que tiveram complicações pós-operatórias era maior (p=0.0006), assim como entre os doentes que morreram (p=0.0041). A tabela 2 apresenta os resultados cirúrgicos após 30 dias.

A literatura existente sugere que o grau de estenose carotídea e a gravidade da doença carotídea estão relacionadas com o aumento da mortalidade por complicações neurológicas no decorrer e após cirurgia cardíaca, pelo que o tratamento da doença carotídea de base poderá fazer diminuir a incidência de AVC na CRM. Por outro lado, revisões sistemáticas recentes objectivam que outros factores de risco são mais determinantes para esses desfechos neurológicos, como os antecedentes pessoais de AVC e AIT, comparando-os com doentes assintomáticos. As guidelines actuais da

Sociedade Europeia de Cardiologia e da Sociedade Europeia de Cirurgia Vascular são unânimes a considerar que, actualmente, não existe uma estratégia eficaz e consensual para o tratamento de doentes de alto risco cirúrgico com doença carotídea grave concomitante, deixando ao critério da equipa experiente a análise de cada doente individualmente. A única indicação prende-se com uma história pessoas de AVC ou AIT nos 6 meses anteriores à cirurgia cardíaca, em doentes com estenose da artéria carótida interna superior a 70%, na qual há uma indicação clara para a CEA. O próprio timing da CEA é alvo de estudo e debate, sendo que múltiplos estudos comprovaram a segurança do procedimento síncrono, às vezes até superior, quando comparado ao procedimento escalado. De acordo com os nossos resultados obtidos, não encontramos diferenças estatisticamente significativas tanto na taxa de complicações major (determinadas pela ocorrência de falência multi-orgânica, enfarte agudo do miocárdio, choque cardiogénico, pneumonia, mediastinite, lesão renal aguda e hematoma cervical, que tivesse implicado uma estadia na Unidade de Cuidados Intensivos superior a 5 dias) quanto na taxa de mortalidade global nos dois grupos de estudo (8.1% de AVC+morte no grupo 1 *versus* 7% no grupo 2, p=0.524). Mesmo no grau de gravidade da doença carotídea, não foram encontradas diferenças estaticamente significativas para os outcomes neurológicos entre os dois grupos populacionais. Por outro lado, no estudo de comparação das complicações major pós-cirúrgicas, observou-se que os doentes que tiveram complicações tinham um Euroscore superior aos que não tiveram (11.49 *vs* 7.86, p=0.0006), enquanto que entre os doentes que morreram o Euroscore era também estatisticamente diferente dos que sobreviveram (12.74 vs 8.21, p=0.0041). Estes dados demonstram que os doentes com estenose carotídea têm outras co-morbilidades que influenciam o seu Euroscore e que a mortalidade está também relacionada com essas doenças de base e com seu estado de saúde precário, o que está em consonância com a literatura mais actual.

Em conclusão, o nosso estudo demonstra que a cirurgia síncrona, quando efectuada por uma equipa experiente, não obteve riscos cirúrgicos adversos, comparáveis às intervenções escaladas. O grau de estenose não parece ter um impacto significativo na taxa de mortalidade e AVC pós-cirúrgicos, contudo o Euroscore, que é bastante elevado no nosso grupo de estudo, demonstra que os doentes estão em maior risco de complicações, independentemente do tipo e complexidade de cirurgia cardíaca realizada. A revascularização carotídea síncrona parece ter um impacto positivo na prevenção de AVC ipsilateral.

## REFERENCES

[1] Naylor AR, Mehta Z, Rothwell PM, Bell PR. Carotid artery disease and stroke during coronary artery bypass: a critical review of the literature. Eur J Vasc Endovasc Surg; 23 (2002), pp. 283–294.

[2] Steinvil A, Sadeh B, Arbel Y, et al. Prevalence and predictors of concomitant carotid and coronary artery atherosclerotic disease. J Am Coll Cardiol; 57 (2011), pp. 779–783.

[3] Schwartz LB, Bridgman AH, Kieffer RW, et al. Asymptomatic carotid artery stenosis and stroke in patients undergoing cardiopulmonary bypass. J Vasc Surg; 21 (1995), pp. 146–153.

[4] Das SK, Brow TD, Pepper J. Continuing controversy in the management of concomitant coronary and carotid disease: an overview. Int J Cardiol; 74 (2000), pp. 47–65.

[5] Ascher E, Hingorani A, Yorkovich W, Ramsey PJ, Salles-Cunha S. Routine pre-operative carotid duplex scanning in patients undergoing open-heart surgery: is it worthwhile? Ann Vasc Surg; 15 (2001), pp. 669–678.

[6] Barnes RW, Marszalek PB. Asymptomatic carotid disease in the cardiovascular surgical patient: is prophylactic endarterectomy necessary? Stroke; 12 (1981), pp. 497–500.

[7] Beauford RB, Saunders CR, Goldstein DJ. Off pump concomitant coronary revascularization and carotid endarterectomy. J Cardiovasc Surg; 44 (2003), pp. 407–415.

[8] Durand DJ, Perler BA, Roseborough GS, Grega MA, Borowicz LM, Baumgartner WA. Mandatory versus selective pre-operative carotid screening: a retrospective analysis. Ann Thorac Surg; 78 (2004), pp. 159–166.

[9] Dworschak M, Czerny M, Grimm M, Grubhofer G, Plochl W. The impact of asymptomatic carotid artery disease on the intraoperative course of coronary bypass surgery. Perfusion; 18 (2003), pp. 15–18.

[10] Naylor AR, Bown MJ. Stroke after cardiac surgery and its association with asymptomatic carotid disease: an updated systematic review and meta-analysis. Eur J Vasc Endovasc Surg; 41 (2011), pp. 607–624.

[11] Naylor AR, Mehta Z, Rothwell PM, Bell PR. Carotid artery disease and stroke during coronary artery bypass: a critical review of the literature. Eur J Vasc Endovasc Surg; 23 (2002), pp. 283- 294.

[12] Dönmez AA, Adademir T, Sacli H, Koksal C, Alp M. Comparison of Early Outcomes with Three Approaches for Combined Coronary Revascularization and Carotid Endarterectomy. Braz J Cardiovasc Surg.; 31 (2016), pp. 365-370.

[13] Ricotta JJ, Char DJ, Cuadra SA, Bilfinger TV, Wall LP, Giron F, et al. Modeling stroke risk after coronary artery bypass and combined coronary artery bypass and carotid endarterectomy. Stroke; 5 (2003), pp. 1212–1217.

[14] Schwartz LB, Bridgman AH, Kiefer RW, Wilcox RA, McCann RL, Tawi MP, Scott SM. Asymptomatic carotid artery stenosis and stroke in patients undergoing cardiovascular bypass, J Vasc Surg; vol. 21 (1995), pp. 146 -153.

[15] Das SK, Brow TD, Pepper J. Continuing controversy in the management of concomitant coronary and carotid disease: an overview, International Journal of Cardiology; vol. 74 (2000), pp. 47-65.

[16] Salasidis GC, Latter DA, Steinmetz OK, Blair JF, Graham AM. Carotid artery duplex scanning in preoperative assessment for coronary artery revascularization, J Vasc Surg; vol. 21 (1995), pp. 154 -161.

[17] Naylor AR, Mehta Z, Rothwell PM, Bell PR. Carotid artery disease and stroke during coronary artery bypass: A critical review of the literature. Eur J Vasc Endovasc Surg.; 23 (2002), pp. 283–294.

[18] Barbut D, Grassineau D, Lis E, Heier L, Hartman G. Posterior distribution of infarcts in strokes related to cardiac operations. Ann Thorac Surg.; 65 (1998), pp. 1656-1659.

[19] Li Y, Walicki D, Mathiesen C, Jenny D, Li Q, Isayev Y, Reed JF, Castaldo JE. Strokes After Cardiac Surgery and Relationship to Carotid Stenosis. Arch Neurol.; 66

(2009), pp. 1091-1096.

[20] Mahmoudi M, Hill PC, Xue Z, Torguson R, Ali G, Boyce SW, et al. Patients with severe asymptomatic carotid artery stenosis not have a higher risk of stroke and mortality after coronary artery bypass surgery. Stroke; 42 (2011), pp. 2801–2805.

[21] Adams B, et al. There is No Benefit to Universal Carotid Artery Duplex Screening before a Major Cardiac Surgical Procedure. Ann Vasc Surg.; 28 (2014), pp. 93–101.

[22] Gaudino M, et al. Should severe monolateral asymptomatic carotid artery stenosis be treated at the time of coronary artery bypass operation? Eur J Cardiothorac Surg.; 19 (2001), pp. 619–626.

[23] Ghosh J, Murray D, Khwaja N, et al. The influence of asymptomatic significant carotid disease on mortality and morbidity in patients undergoing coronary artery bypass surgery. Eur J Vasc Endovasc Surg.; 29 (2005), pp. 88-90.

[24] Van der Heyden J, Plokker HW. Part Two: Against the motion. Carotid disease is responsible for the increased risk of stroke after coronary bypass surgery. Eur J Vasc Endovasc Surg.; 40 (2010), pp. 693–695.

[25] 2014 ESC/EACTS Guidelines on Myocardial Revascularization.

[26] Chaturvedi S, Bruno A, Feasby T, Holloway R, Benavente O, Cohen SN, Cote R, Hess D, Saver J, Spence JD, Stern B, Wilterdink J. Carotid endarterectomy: an evidence-based review: report of the Therapeutics and Technology Assessment Subcommittee of the American Academy of Neurology. Neurology; 65 (2005), pp. 794–801.

[27] Wijeysundera DN, et al. Off-pump coronary artery surgery for reducing mortality and morbidity. Meta-analysis of randomized and observational studies. J Am Coll Cardiol.; 46 (2005), pp. 872-882.

[28] Cheng DC, Bainbridge D, Martin JE, Novick RJ. The Evidence-based Perioperative Clinical Outcomes Research Group. Does off-pump coronary artery bypass reduce mortality, morbidity and resource utilization when compared with conventional coronary artery bypass? A meta-analysis of randomized

trials, Anesthesiology; 102 (2005), pp. 188-203.

[29] Bucerius J, Gummert JF, Borger MA, Walther T, Doll N, Onnasch JF, Metz S, Falk V, Mohr FW. Stroke after cardiac surgery: a risk factor analysis of 16,184 consecutive adult patients, Ann Thorac Surg.; 75 (2003), pp. 472-478.

[30] Lamy A, Devereaux PJ, Prabhakaran D, Taggart DP, Hu S, Paolasso E, Straka Z, Piegas LS, Akar AR, Jain AR, Noiseux N, Padmanabhan C, Bahamondes JC, Novick RJ, Vaijyanath P, Reddy S, Tao L, Olavegogeascoechea PA, Airan B, Sulling TA, Whitlock RP, Ou Y, Ng J, Chrolavicius S, Yusuf S. Effects of Off-Pump and On-Pump Coronary-Artery Bypass Grafting at 1 Year. N Engl J Med; 368 (2013), pp. 1179–1188.

[31] Meharwal ZS, Mishra A, Trehan N. Safety and efficacy of one stage off-pump coronary artery operation and carotid endarterectomy. Ann Thorac Surg.; 73 (2002), pp. 793–797.

[32] Ogutu P, Werner R, Oertel F, Beyer M. Should patients with asymptomatic significant carotid stenosis undergo simultaneous carotid and cardiac surgery? Interact Cardiovasc Thorac Surg.; 18 (2014), pp. 511–518.

[33] Paciaroni M, Caso V, Acciarresi M, Baumgartner RW, Agnelli G. Management of asymptomatic carotid stenosis in patients undergoing general and vascular surgical procedures. J Neurol Neurosurg Psychiatry; 76 (2005), pp. 1332–1336.

[34] Garg et al. Combining carotid endarterectomy with off-pump coronary artery bypass graft surgery is safe and effective. Ann Indian Acad Neurol.; 18 (2015), pp. 419–423.

[35] Dönmez AA, Adademir T, Sacli H, Koksal C, Alp M. Comparison of Early Outcomes with Three Approaches for Combined Coronary Revascularization and Carotid Endarterectomy. Braz J Cardiovasc Surg.; 31 (2016), pp. 365-370.

[36] Sharma V, Deo SV, Park SJ, Joyce LD. Meta-analysis of staged versus combined carotid endarterectomy and coronary artery bypass grafting. Ann Thorac Surg.; 97 (2014), pp. 102-109.

[37] Paraskevas KI., Nduwayo S, Saratzis A, Naylor AR, A Systematic Review and

Meta-analysis of Outcomes Following Staged/Synchronous Carotid Artery Stanting and Coronary Artery Bypass Surgery. European Journal of Vascular and Endovascular Surgery; 2016.

[38] Lin et al. Clinical utility of carotid duplex ultrasound prior to cardiac surgery. Journal of Vascular Surgery; 63 (2016), pp. 709-714.

# AGRADECIMENTOS

Quero agradecer, em primeiro lugar, o apoio do Professor Doutor Luís Mendes Pedro, orientador deste Trabalho Final de Mestrado, cuja motivação e espírito crítico se mostraram fulcrais para o desenvolvimento deste trabalho. Agradeço-lhe o desafio e espero que seja possível colaborarmos novamente no futuro.

Em segundo lugar, agradeço o imprescindível suporte do Dr. Tony Soares, que me ajudou com o estudo estatístico e com a organização deste trabalho.

Em terceiro lugar, agradeço ao meu Pai por todos os esforços realizados durante este percurso académico. Agradeço o apoio e motivação incessantes ao longo dos últimos seis anos.