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Operative- and Long-Term Outcomes of Combined and Staged Carotid Endarterectomy and Coronary Bypass

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Abstract

Objective: Optimal temporal surgical management of significant carotid stenosis (CS) and coronary artery disease (CAD) remains unknown. Carotid endarterectomy (CEA) and coronary bypass (CABG) are performed concurrently (CCAB) or in staged (CEA-CABG or CABG-CEA) approach. Using the Vascular Quality Initiative (VQI)-Vascular Implant Surveillance and Interventional Outcomes Coordinated Registry Network (VISION)-Medicare linked dataset, this study compared operative and long-term outcomes following CCAB and staged approaches.

Methods: The VQI-VISION dataset was used to identify CEAs from 2011 to 2018 with combined CABG or CABG within 45 days preceding or following CEA. Patients were stratified based on concurrent or staged approach. Primary outcomes were stroke, myocardial infarction (MI), all-cause mortality, stroke and death as composite (SD) and all as composite (SMD) within 30-days from the last procedure as well as long-term. Univariate analysis and risk-adjusted analysis using inverse propensity weighting (IPW) were performed. Kaplan-Meier curves of stroke, MI, and death were created and compared.

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Results: There were 1,058 patients included: 643 CCAB and 415 staged (309 CEA-CABG and 106 CABG-CEA). Compared to staged patients, those undergoing CCAB had a higher preoperative rate of congestive heart failure (24.8% vs 18.4%, $p=0.01$) and decreased renal function (14.9% vs 8.5%, $p<0.01$) as well as fewer prior neurological events (23.5% vs 31.4%, $p<0.01$). Patients undergoing CCAB had similar weighted rates of 30-day stroke (4.6% vs 4.1%, $p=0.72$), death (7.0% vs 5.0%, $p=0.32$), and composite outcomes (SD: 9.8% vs 8.5%, $p=0.56$; SDM: 14.7% vs 17.4%, $p=0.31$) but a lower weighted rate of MI (5.5% vs 11.5%, $p<0.01$) versus the staged cohort. Long-term adjusted risks of stroke (HR, 0.85; 95% CI, 0.54 – 1.36; $p=0.51$) and mortality (HR, 1.02; 95% CI, 0.76 – 1.36; $p=0.91$) were similar between groups, but higher risk of MI long-term was seen in those staged (HR, 1.49; 95% CI, 1.07 – 2.08; $p=0.02$).

Conclusions: In patients undergoing CCAB or staged open revascularization for CS and CAD, the staged approach had increased risk of postoperative cardiac event, but short- and long-term rates of stroke and mortality appear comparable. Adverse cardiovascular event risk is high between operations when staged and should be a consideration when selecting an approach. Although factors leading to staged sequencing performance need further clarity, CCAB appears safe and should be considered an equally reasonable option.

Table of Contents Summary

In this retrospective analysis of the VQI-VISION Medicare-Linked database authors found similar rates of stroke, death, and composite, but lower rate of MI in combined CEA and CABG compared to a staged. When disease falls within accepted guidelines, combined approach should be considered an equally reasonable option at capable centers.

Introduction:

It is believed that up to 22% of patients with significant coronary artery disease have carotid stenosis that requires intervention.^{1,2} Similarly, in patients undergoing coronary artery bypass grafting (CABG), the prevalence of >50% carotid stenosis is 9% and >80% stenosis is 7%.³ There is debate regarding the optimal temporal management of carotid and coronary disease. The most effective temporal management to reduce risk and treat both territories remains unclear. There are those advocating for a combined approach, with a combined carotid endarterectomy (CEA) and coronary artery bypass grafting (CABG) performed in the same setting. Alternatively, some feel that a staged approach is superior. The optimal sequenced order of the two procedures within a staged approach is also under debate with some in favor of CABG followed by CEA and others recommending the reverse.

Undoubtedly, patient selection and center experience play a role in this decision-making process. It has been shown that centers with experience in CCAB attain outstanding results.⁴ Many suggest that CCAB is appropriate in patients with both symptomatic cardiac disease and carotid stenosis.^{1,4-6} Similar arguments for CCAB have been made in patients with symptomatic cardiac disease and asymptomatic carotid stenosis with contralateral occlusion, bilateral asymptomatic disease, or severe unilateral pre-occlusive lesions.^{7,8} These have been given some consideration in recent guidelines.³⁻⁵ However, these arguments are based largely on single center or regional experience,⁸⁻¹⁰ comparing the risk of CCAB to isolated CABG and isolated CEA,¹⁰⁻¹³ or on larger registries and meta-analyses with lack of

appropriate granularity.^{1,14–16} Few studies have performed direct comparisons of CCAB to staged approaches in the management of significant carotid stenosis and coronary artery disease.

Using the Vascular Quality Initiative (VQI)-Vascular Implant Surveillance and Interventional Outcomes Coordinated Registry Network (VISION) (VQI-Medicare linked dataset), this study compared operative and long-term outcomes following CCAB and staged approaches in the management of significant carotid stenosis and coronary artery disease. We hypothesized that there would be no difference in outcomes when comparing CCAB to staged approaches.

Methods:

Analytic cohort

Using the VQI-VISION dataset,¹⁷ we identified patients undergoing CEA from January 1st, 2011 to December 31st, 2018, with combined CABG or CABG within 45 days preceding or following CEA. The use of VQI-VISION was approved by Weill Cornell Medicine Institutional Review Board and informed consent was waived. Exclusion criteria are shown in Figure 1. Patients were excluded if they did not have Medicare entitlement during the concurrent procedure, or with discontinued entitlement between the staged procedure. Additional exclusion criteria include traumatic carotid injury, prior transplant, concurrent structural heart procedure, concurrent proximal or distal carotid endovascular procedures. Patients were stratified based on the timing of CABG and grouped as having a concurrent (CCAB) or a staged approach. For the primary analysis, the staged approach included both possible sequences — CEA-CABG and CABG-CEA. In the subgroup analysis, we examined CEA-CABG and CABG-CEA sequencing separately. Within the staged cohort, further stratification was carried out based on the time between the first and second procedure –less than or equal to 7 days (staged early) and greater than 7 days (staged late). Finally, all patients were stratified based on symptomatic or asymptomatic carotid status which was defined by the presence or absence of prior neurologic event. Baseline demographics were identified from Medicare claims and VQI. Definitions of medical comorbidities and procedure details within VQI over the study period were used.¹⁸ Operative details pertaining to CABG and cardiopulmonary bypass were determined using ICD 9 and ICD 10 procedure codes.

Outcomes

Short and long-term outcomes were identified from Medicare claims. Primary endpoints were perioperative occurrence of stroke, death, myocardial infarction (MI), and these as composite (SD and SDM). A perioperative outcome was defined as an event happening within 30 days following CCAB or within 30 days following the second procedure in the staged cohort. Stroke was determined by a stroke diagnosis accompanied by head CTs. Mortality was determined based on death dates in the Medicare Master Beneficiary Summary File. MI was identified based on diagnosis codes during the admission for the CABG and CEA procedures and subsequent claims. For MI diagnoses present during the admission of the CCAB or the staged procedure, those indicated as not present-on-admission

were considered postoperative. Events between staged procedures were also identified. Long-term incidences of stroke, death, and MI were also evaluated and compared between groups. Patients were censored at the end of the study (December 31, 2018) or when they stopped enrolling in fee-for-service Medicare, whichever was earlier.

Statistical methods

Patients' age was presented with median and interquartile range and was compared with the Wilcoxon Rank-sum test across CCAB and staged groups. Categorical variables were presented with counts and percentages and were compared with the Chi-square test or Fisher's exact test. In the unadjusted analysis, we used logistic regressions to compare the risk of 30-day events between patients receiving CCAB and those receiving a staged approach. For long-term outcomes, we performed Kaplan-Meier analysis and Cox proportional hazards models. Inverse probability weighting was used to adjust for differences in baseline characteristics. We selected a subset of baseline characteristics into a logistic regression model to estimate the propensity of receiving staged procedures and calculate the inverse probability treatment weight for each patient. Standardized mean differences were calculated for each variable included in the propensity model to evaluate the cohort balance before and after weighting. We estimated weighted event rates and compared them with the Rao-Scott Chi-Square test. Generalized linear models and Cox regression models with robust sandwich estimators were used to compare the risk of events accounting for the weighted cohort. A p value of < 0.05 was considered significant. Outcome groups with less than 11 patients were censored due to Medicare data use agreement and these are represented as < 11. All analyses were performed in SAS 9.4 (Cary, NC).

Results:

Baseline and operative characteristics

We identified 1058 patients from the VQI-Medicare linked VISION database who underwent concurrent or staged CEA and CABG and did not meet any exclusion criteria. Of these, 643 underwent CCAB and 415 underwent a staged approach. Within the staged cohort, there were 309 who underwent CEA-CABG and 106 who underwent CABG-CEA (Figure 1). In the CEA-CABG cohort the median number of days between procedures was 5 (interquartile range 2–17). In the CABG-CEA cohort the median number of days between procedures was 26 (interquartile range 7–38). Compared to patients undergoing a staged approach, patients undergoing CCAB had lower rates of prior neurological event (23.5% vs 31.4%) and preserved ambulatory status (78.2% vs 84.6%), but also higher rates of congestive heart failure (24.8% vs 18.4%) and decreased renal function (creatinine >1.5mg/dl, 14.9% vs 8.5%). There was no difference in cardiac or coronary medical optimization between groups (e.g., aspirin, statin, P2Y inhibitor, anticoagulation). Evaluation of operative factors revealed a higher rate of CABG on cardiopulmonary bypass in CCAB compared to staged (78.8% vs 46.7%) (Table 1).

Perioperative outcomes

Postoperative events were compared between CCAB and staged cohorts (Table 2). Events occurring within 30 days following the second procedure in the staged cohort were compared to 30-day events following CCAB. Rates of mortality, stroke, and composite outcomes were not significantly different between CCAB and staged groups. However, there was a significantly higher rate of post-operative MI following the second procedure in the staged group (10.1%) compared to CCAB (5.3%). This remained true following inverse proportional weighting adjustment (11.5% vs 5.5%) (Table 2).

Events between CABG and CEA procedures were evaluated within the staged cohort. Of those undergoing a staged approach, 22 (5.3%) patients experienced stroke between first and second procedure and 79 (19%) had MI between procedures. Stroke was more common between CABG-CEA (>11 out of 106 vs <11 out of 309, $p<0.01$) and MI between CEA-CABG (>68 out of 309 vs <11 out of 106, $p<0.01$) sequencing, respectively. Of the 79 patients in the staged group who experienced MI between procedures, 12 patients also had postoperative MI following the second procedure.

Long term outcomes

Long-term outcomes were compared (Table 3, Figure 2). Median (interquartile range) follow up for the entire cohort was 921 days (384 – 1560 days). Median follow up for CCAB was 966 days (376 – 1624 days) and for staged was 871 days (396 – 1408 days). While there was no difference in long-term incidences of stroke, MI, or mortality in the unadjusted analysis, there was a significantly higher long-term incidence of MI in the staged cohort following risk adjustment ($p=0.02$).

Short- and long-term outcomes of staged group stratified by time to second procedure

The staged group was stratified by time to second procedure (staged-early: ≤ 7 days, staged-late: >7 days) and outcomes were each compared to CCAB (Table 4). There were 226 patients in the staged-early group and 189 in the staged-late group. There were no differences in rates of postoperative mortality, stroke, MI, or composite outcomes in the staged-late group compared to CCAB. Risk adjustment was not performed in staged-late compared to CCAB due to low sample size and unbalanced covariates. In the staged-early group there was a significantly higher incidence of postoperative MI compared to CCAB (11.9% vs 5.3%, $p<0.01$). This remained true following risk adjustment (13.4% vs 5.3%, $p<0.01$.) Compared to CCAB, the long-term risks of stroke [HR 0.81 (0.49, 1.36), $p=0.42$] and MI [HR 1.13 (0.76, 1.68), $p=0.55$] were similar in the staged-late group but the mortality risk was significantly lower [HR 0.62 (0.41, 0.93), $p=0.02$] in the staged-late group. In the staged-early group, the long-term risks of mortality [HR 1.06 (0.78, 1.44), $p=0.70$] and stroke [HR 0.68 (0.41, 1.14), $p=0.15$] were similar compared to CCAB but the risk of MI was higher [HR 1.42 (1.01, 2.01), $p=0.05$]. This remained true for MI following risk adjustment [HR 1.64 (1.11, 2.42), $p=0.01$].

Symptomatic carotid status

CCAB and staged groups were further stratified by symptomatic carotid status and risk adjusted outcomes were compared. In the CCAB cohort there were 151 symptomatic

patients and in staged there were 130 symptomatic patients. In symptomatic patients, rates of mortality [16 (5.9%) vs <11, p=0.16], stroke [27 (9.9%) vs 17 (6.5%), p=0.42], MI [17 (6.1%) vs 27 (10.3%), p=0.37], composite SD [36 (13.1%) vs 24 (9.0%), p=0.38], and composite SDM [51 (18.5%) vs 47 (17.8%), p=0.91] were similar between CCAB and staged groups. Weighted long-term incidences of mortality [HR 0.66 (0.34, 1.27), p=0.66], stroke [HR 0.78 (0.36, 1.72), p=0.54], and MI [HR 1.94 (0.94, 3.97), p=0.07] were similar between symptomatic patients undergoing staged and CCAB.

Among patients with asymptomatic carotid disease (CCAB—492, staged—284 patients), there was no difference in risk adjusted mortality [31 (4.1%) vs 28 (3.7%), p=0.76], stroke [39 (5.3%) vs 34 (4.4%), p=0.67], composite SD [59 (8.0%) vs 57 (7.4%), p=0.81] or composite SDM [97 (13.1%) vs 123 (16.0%), p=0.34] between CCAB and staged groups. However, there was a lower rate of MI [43 (5.8%) vs 86 (11.1%), p=0.02] in CCAB group compared the staged group. In patients with asymptomatic carotid disease, long-term risks of mortality [HR 1.2 (0.86, 1.68), p=0.29], stroke [HR 0.98 (0.54, 1.77), p=0.94], and MI [HR 1.47 (1.00, 2.18), p=0.05] were similar between staged and CCAB.

Staged: CEA-CABG and CABG-CEA

Within the staged cohort, patients were stratified by procedure sequence (CEA followed by CABG vs CABG followed by CEA) and unadjusted outcomes were compared (Supplemental Table). There were 309 patients in the CEA followed by CABG group and 106 patients in the CABG followed by CEA group. Although rates of postoperative mortality [<15 vs <11, p=0.37], stroke [<16 vs <11, p=0.38], and composite SD [>19 vs <11, p=0.11] were similar between groups, there was higher incidences of postoperative MI [>31 vs <11, p=0.01] and composite mortality, stroke, and MI [>53 vs <11, p<0.01] in the CEA followed by CABG group compared to the CABG followed by CEA group.

Discussion:

This study uses the recently developed VISION (VQI-Medicare linked dataset) to evaluate outcomes following CEA and CABG in combined and staged fashion. We found no difference in early or late incidence of stroke or mortality in patients undergoing CCAB compared to those undergoing a staged approach. However, there was a higher rate of MI in the staged group compared to the combined group. When stratified by symptomatic carotid status the increased rate of post-operative MI in the staged group was primarily seen in asymptomatic patients. Similarly, increased incidence of post-operative MI was seen in patients undergoing staged procedures where the second procedure occurred less than or equal to 7 days from the first. Within the staged cohort, the higher rate of MI was primarily seen in patients undergoing CEA followed by CABG compared to patients undergoing CABG followed by CEA. These findings will help clarify and guide clinicians in the operative management of patients with both significant carotid and coronary disease.

Complication rates following CCAB found in this study largely align with previously reported rates (mortality 4–5.6%, stroke 3–6.2%, MI 3.6–5%, SD 7.7–9.5%).^{1,3,15,16,19–21} Similarly, those following the staged approach were largely comparable to rates previously reported (mortality 3.8–4.2%, stroke 1.9–3.5%, SD 5.4–7.1%).^{3,14,15} However, our study did

reveal a somewhat higher rate of postoperative stroke (5.0%) following staged approach than others. Current guidelines suggest consideration of CCAB in patients undergoing CABG who have symptomatic carotid disease and ipsilateral carotid stenosis 50–99%.^{3,22,23} CCAB is also considered in those undergoing CABG with asymptomatic bilateral severe carotid stenosis (70–99%) or unilateral severe carotid stenosis with contralateral occlusion.³ The complexity of this patient population cannot be overstated and there has been a great deal of diligent work in the past few decades furthering understanding of management paradigms.^{24–28}

The guidelines above continue to be essentially based on studies demonstrating highest risk of postoperative stroke in CABG patients with symptomatic carotid disease.²⁹ Moreover, previous works have demonstrated an increased incidence of post CABG stroke in patients with carotid occlusion and severe bilateral stenosis.^{7,30} However, even this is debated as some studies suggest no difference in rate of post-operative neurologic outcome following isolated CABG or combined approach in patients with coronary disease and severe carotid disease.¹³ The rationale for CCAB in unilateral asymptomatic carotid disease is even less clear as current evidence does not suggest a robust relationship between unilateral asymptomatic carotid disease and post-CABG stroke or mortality.^{3,13}

Prior queries of administrative datasets focus on stroke, mortality, and SD composite as primary outcomes.^{13–15,31} As we found no difference in the short- or long-term incidence of stroke, death, or SD between staged or combined approaches, our study confirms findings by Gopaldas and colleagues following an examination of the Nationwide Inpatient Sample (NIS) from 1998–2007.¹⁵ In another study evaluating patients undergoing CCAB and staged procedures from the NIS between 2004–2012, the adjusted risk of death or stroke was also similar between groups.¹⁴ Recent meta-analyses, however, have conflicting outcomes. Some suggest worse neurologic outcomes with CCAB compared to staged.^{19,32,33} A prospective study by Oz and colleagues assigned patients to either combined approach or CEA 1 week prior to CABG and found higher rates of adverse neurologic events and increased mortality in the combined approach.²¹ However, unstable cardiac status was the primary indication to assign patients to the combined approach in this study so the worse outcomes in this group are not surprising. Other studies indicate similar rates of stroke and/or death in combined and staged approaches.^{1,16} This present study would support similar rates with either strategy, and further, also the current guidelines.

Fewer studies examine the impact of CCAB and staged surgical algorithms on the incidence of postoperative MI. Utilization of the VISION (VQI-Medicare linked dataset) afforded this possibility. While we found no difference in the incidence of stroke, death, or SD between CCAB and staged, we did see an increased incidence of postoperative MI in the staged group compared to CCAB. This was present in both short- and long-term analysis. The differences in the long-term appear to be primarily driven by the short-term outcomes. We did not include events between staged procedures in these postoperative outcomes to prevent risk time bias. There was a 5.3% cardiovascular event rate, mostly MI, between staged procedures adding to risk. Increased risk of myocardial events in staged patients has also been appreciated in meta-analysis.^{32,33} Although major guidelines and outcomes of any intervention on carotid stenosis should focus on stroke and death as the implicit marker of

success, these findings, underline the importance of appreciating post-operative MI risk in staged approaches.

Following risk adjustment and stratification by symptomatic carotid status, the comparative increase in post-operative MI in the staged group was most pronounced in asymptomatic carotid patients. This finding was somewhat surprising, particularly since most assessments of patients with combined carotid, coronary disease indicate similar or worse myocardial ischemic events in symptomatic carotid patients.¹¹ In our data, severe bilateral disease was more common in the asymptomatic group, which is obviously considered for CCAB in recent guidelines.^{3,22,23} Better understanding of those with higher MI risk is needed. We suspected that symptomatic carotid status would affect stroke outcomes but our data does not support this. The database does not provide information regarding type of symptoms, laterality, and temporal relationship between carotid symptom onset and operative intervention. This information is important in future evaluation.

While our study is somewhat underpowered to compare these sub-cohorts and additional work is needed, a shorter duration between procedures (staged-early: 7 days) in the staged group and the sequenced order of procedures within the staged group also had an impact on outcome. Incidence of MI as well as composite SDM were higher in the CEA-CABG sequence compared to CABG-CEA. A similar pattern for postoperative cardiac complications has been previously described.^{15,20} In a systematic review, Naylor and colleagues described a 6.5% incidence of MI following CEA-CABG sequence and 0.9% following CABG-CEA sequence. Intuition suggests this phenomenon might be related to optimizing cardiac risk up front in the CABG-CEA sequence. However, these groups are not equivalent, and they represent different entities with distinct risk profiles. Additionally, events in between procedures could confound this analysis as the indication for the coronary procedures, especially when CABG is the latter in the staged sequence, is difficult to ascertain herein. For example, there were a subset of patients who experienced post-operative MI following CEA potentially leading to CABG within 45 days that may not have been planned. Conversely, there were patients who experienced post-operative neurologic complication following primary CABG and then underwent subsequent CEA within 45 days. Despite these possible confounders there was no difference in overall incidence of stroke between the two staged sequences. Previous studies have demonstrated increased incidence of stroke in the CABG-CEA sequence.¹⁵ Interestingly, the time between staged procedures was longer in the CABG-CEA sequence. This likely is related to lengthier recovery times following CABG compared to CEA.

In addition to CEA, contemporary operative management of carotid disease now includes CAS and TCAR. These were not included in the present analysis due to low sample size at the current time, but may have a significant impact on management going forward. As these minimally invasive procedures become more widespread, centers may be more willing to consider combined management of significant coronary and carotid disease. As such, this may alter the preferred approaches to combined carotid, coronary disease in the future.

This study has limitations to consider. The study is limited by its retrospective nature and those inherent with large database analysis (e.g. entry errors and missing data). We

were limited by database sample size especially where comparing sub-cohorts. Our study introduces inherent differences in these sub-groups but additional work with greater power is needed to make durable comparison. It is clear from the demographics that our study includes a predominance of white male patients. Thus, our findings may not be applicable to all patients. There are more patients in the CEA-CABG sequence compared to the inverse. Perhaps this is due to differences in screening practices and preoperative optimization in patients with known coronary compared to carotid disease. The lack of information regarding timing and laterality of prior neurologic events is also a limitation of this work. Though risk adjustment was performed, it is possible that additional confounders exist. Some degree of selection bias is likely present in our cohort as only patients in the staged group were identified and included if they had both procedures performed. Thus, a major limitation is lack of knowledge of preoperative intent. For example, we did not identify or include patients who were intended to have a staged approach in the management of severe carotid stenosis and CAD but did not have the second procedure-potentially because of complication following the first. Conversely, there is also a subgroup within the staged cohort who may not have been initially intended to undergo both procedures within 45 days—likely driven by complication. Additional work is needed to better understand and identify intention to treat for combined disease in larger datasets.

Conclusion

In conclusion, there was no difference in early or late incidence of stroke or death in patients undergoing CCAB compared to those undergoing staged approach. However, there was a higher rate of MI in the staged group. Also, there is defined risk of stroke and MI between staged cases. Our findings highlight the importance of understanding postoperative MI in these patients in addition to stroke and death. Finally, we feel that CCAB is safe, and if disease falls within accepted guidelines should be considered an equally reasonable, if not superior, option at capable centers.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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ARTICLE HIGHLIGHTS**Type of Research:**

Retrospective analysis of prospectively collected Vascular Quality Initiative (VQI)-Vascular Implant Surveillance and Interventional Outcomes Coordinated Registry Network (VISION) (VQI-Medicare linked dataset) data

Key Findings:

Compared to the staged approach (415 patients), patients undergoing combined carotid endarterectomy and coronary artery bypass grafting (643 patients) had similar rate of 30-day stroke (4.6% vs 4.1%, $p=0.72$), 30-day death (7.0% vs 5.0%, $p=0.32$), and 30-day composite outcomes (Stroke/Death: 9.8% vs 8.5%, $p=0.56$; Stroke/Death/MI: 14.7% vs 17.4%, $p=0.31$) but a lower rate of 30-day MI (5.5% vs 11.5%, $p<0.01$).

Take home Message:

Compared to the staged approach, combined carotid endarterectomy is safe and if disease falls within accepted guidelines should be considered an equally reasonable option at capable centers.

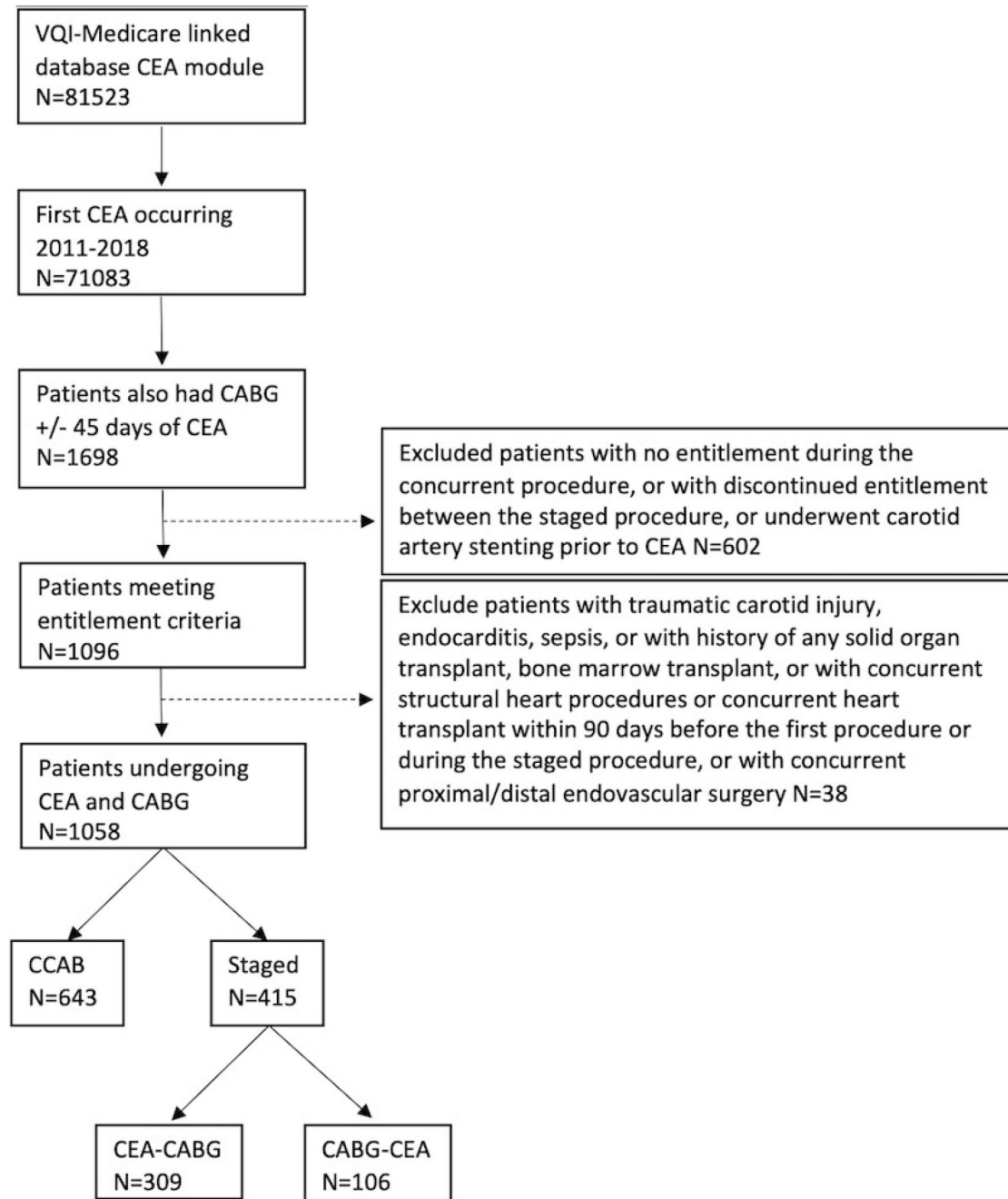


Figure I:
Flowchart demonstrating inclusion and exclusion criteria

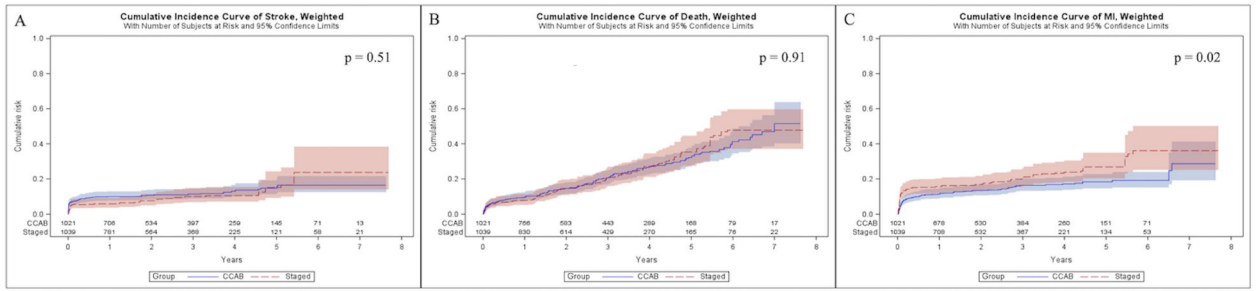


Figure II:
Cumulative long-term incidence curves of stroke (A), death (B), and MI (C) in CCAB compared to staged, with number of subjects at risk and 95% confidence limits.

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Table I:

Baseline and operative characteristics of patients undergoing concurrent (CCAB) or staged carotid endarterectomy and coronary artery bypass grafting

	CCAB N=643	Staged N=415	p value
Age: median (IQR)	73(68–78)	73(68–77)	0.35
Male	445(69.2%)	308(74.2%)	0.08
White	597(92.8%)	379(91.3%)	0.37
Surgery year			0.03
2011–2013	204(31.7%)	102(24.6%)	
2014–2016	262(40.7%)	176(42.4%)	
2017–2018	177(27.5%)	137(33.0%)	
Smoke			0.69
Never	167(26.1%)	118(28.4%)	
Prior	331(51.6%)	209(50.4%)	
Current	143(22.3%)	88(21.2%)	
HTN	589(91.7%)	384(92.5%)	0.64
Diabetes	283(44.1%)	188(45.3%)	0.70
CHF	159(24.8%)	76(18.4%)	0.01
COPD	151(23.6%)	96(23.1%)	0.86
Renal function			<0.01
Dialysis	17(2.7%)	12(2.9%)	
Creatinine > 1.5mg/dl	95(14.9%)	35(8.5%)	
Creatinine ≤ 1.5mg/dl	527(82.5%)	366(88.6%)	
Ambulation status			0.02
Full	503(78.2%)	351(84.6%)	
Other	66(10.3%)	35(8.4%)	
Missing	74(11.5%)	29(7.0%)	
Living status			1
Home	11	11	
Nursing home/homeless	<11	<11	
Preop statin	519(81.0%)	352(84.8%)	0.11
Preop ASA	532(82.9%)	346(83.4%)	0.83
Preop P2Y	131(20.4%)	100(24.2%)	0.15
Preop anticoagulation			0.11
Yes	58(9.0%)	38(9.2%)	
No	517(80.4%)	349(84.1%)	
Missing	68(10.6%)	28(6.7%)	
Preop beta blocker	512(80.0%)	329(79.3%)	0.78
Preop ACE			0.05
Yes	275(42.8%)	200(48.2%)	
No	299(46.5%)	187(45.1%)	
Missing	69(10.7%)	28(6.7%)	

	CCAB N=643	Staged N=415	p value
Prior neurologic event	151(23.5%)	130(31.4%)	<0.01
Ipsilateral stenosis			0.45
50	<11	<11	
>50 – 70	45(7.0%)	32(7.7%)	
>70	456(70.9%)	275(66.3%)	
Occluded	11	<11	
Missing	125(19.4%)	95(22.9%)	
Contralateral stenosis			0.43
50	211(32.8%)	142(34.2%)	
>50 – 70	145(22.6%)	84(20.2%)	
>70	119(18.5%)	71(17.1%)	
Occluded	31(4.8%)	14(3.4%)	
Missing	137(21.3%)	104(25.1%)	
High risk			0.05
Yes	12(1.9%)	<11	
No	559(86.9%)	379(91.3%)	
Missing	72(11.2%)	11	
Protamine	439(68.5%)	289(69.6%)	0.69
Dextran	32(5.0%)	28(6.8%)	0.23
Urgency			0.67
Elective	470(73.2%)	308(74.4%)	
Urgent/Emergent	172(26.8%)	106(25.6%)	
CABG on CPB	507(78.8%)	194(46.7%)	<0.001
Neck radiation	<11	<11	0.22

<11 missing in each of the following variables: smoke, HTN, Diabetes, CAD, CHF, COPD, stress test, living status, preop statin, ASA, P2Y, beta blocker, prior neurologic event, Protamine, Dextran, Urgency, Renal function

Table II:

Post-operative 30-day outcomes of patients undergoing CCAB and staged procedures.

	CCAB N=643	Staged N=415	p value
Mortality	29(4.6%)	15(3.6%)	0.46
Stroke	43(6.8%)	16(3.9%)	0.05
MI	34(5.3%)	42(10.1%)	<0.01
Stroke/Death	61(9.6%)	30(7.2%)	0.19
Stroke/Death/MI	90(14.1%)	64(15.4%)	0.56

Risk-adjusted post-operative outcomes following CCAB and staged procedures			p value *
Mortality	47(4.6%)	43(4.1%)	0.72
Stroke	71(7.0%)	52(5.0%)	0.32
MI	55(5.5%)	119(11.5%)	<0.01
Stroke/Death	99(9.8%)	88(8.5%)	0.56
Stroke/Death/MI	148(14.7%)	181(17.4%)	0.31

* p value from Rao-Scott Chi-Square test

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Table III:

Hazard ratio of long-term events comparing patients undergoing staged procedures to those undergoing CCAB

	Unadjusted	p value	Weighted	p value
Mortality	0.86(0.66, 1.12)	0.27	1.02(0.76,1.36)	0.91
Stroke	0.74(0.50, 1.11)	0.14	0.85(0.54,1.36)	0.51
MI	1.29(0.96, 1.73)	0.09	1.49(1.07, 2.08)	0.02

Adjusted analysis used inverse weight and robust sandwich estimator

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Table IV:

Postoperative 30-day outcomes of patients undergoing CCAB compared to staged early and staged late.

	CCAB N=643	Staged-early N=226 (CEA-CABG 191, CABG- CEA 35)	p value CCAB vs. staged-early	Staged-late N=189 (CEA- CABG 118, CABG- CEA 71)	p value CCAB vs. staged-late
Mortality	29(4.6%)	<15	0.85	<11	0.13
Stroke	43(6.8%)	<11	0.13	<11	0.12
MI	34(5.3%)	27(11.9%)	<0.01	15(7.9%)	0.18
Stroke/Death	61(9.6%)	19(8.4%)	0.60	11(5.8%)	0.11
Stroke/Death/MI	90(14.1%)	41(18.1%)	0.15	23(12.2%)	0.49

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