Title

Effects of timing on in-hospital and one-year outcomes after transcarotid artery revascularization

Journal

Journal of Vascular Surgery, 73(5)

ISSN

0741-5214

Authors

Cui, Christina L
Dakour-Aridi, Hanaa
Eldrup-Jorgensen, Jens
et al.

Publication Date

2021-05-01

DOI

10.1016/j.jvs.2020.08.148

Peer reviewed

HHS Public Access

Author manuscript

J Vasc Surg. Author manuscript; available in PMC 2022 May 01.

Published in final edited form as:

J Vasc Surg. 2021 May ; 73(5): 1649–1657.e1. doi:10.1016/j.jvs.2020.08.148.

Effects of Timing on In-hospital and One-year Outcomes after TransCarotid Artery Revascularization

Christina L. Cui, BS[1], **Hanaa Dakour-Aridi, MD**[1], **Jens Eldrup-Jorgensen, MD**[2], **Marc L. Schermerhorn, MD**[3], **Jeffrey J. Siracuse, MD, MBA**[4], **Mahmoud B. Malas, MD, MHS, FACS**[1]

[1]University of California San Diego, San Diego, CA, USA

[2]Maine Medical Center, Portland, ME, USA

[3]Beth Israel Deaconess Medical Center, Boston, MA, USA

[4]Boston University, Boston Medical Center, Boston, MA, USA

Abstract

Objective: Current recommendations are to perform carotid endarterectomy (CEA) within two weeks of symptoms due to superior long-term stroke prevention, although urgent CEA within 48-hours has been associated with increased perioperative stroke. With the development and rapid adoption of TransCarotid Artery Revascularization (TCAR), we aim to study the impact of timing on outcomes after TCAR.

Methods: Symptomatic patients undergoing TCAR in the Vascular Quality Initiative between September 2016 and November 2019 were stratified by time to procedure: urgent (TCAR within 48-hours), early (TCAR between 3–14 days after symptoms), and late (TCAR greater than 14 days after symptoms). Primary outcome was in-hospital rates of stroke/death and evaluated using logistic regression. Secondary outcome was one-year rate of recurrent ipsilateral stroke and mortality, analyzed using Kaplan Meier Survival Analysis.

Results: A total of 2608 symptomatic patients undergoing TCAR were included: 144 urgent (5.52%), 928 early (35.58%), and 1536 (58.90%) late. Patients undergoing urgent intervention had increased risk of in-hospital stroke/death that was driven primarily by increased risk of stroke. No differences were seen in in-hospital death. On adjusted analysis, urgent intervention had a 3-fold increased odds of stroke [OR:2.8, 95%CI:1.3–6.2, p=0.01] and a 3-fold increased odds of stroke/death [OR:2.9, 95%CI:1.3–6.4, p=0.01] when compared to late intervention. Patients undergoing early intervention had comparable risks of stroke [OR:1.3, 95%CI:0.7–2.3, p=0.40] and stroke/death [OR:1.2, 9%CI:0.7–2.1, p=0.48] when compared to late intervention. On subset analysis, the type of presenting symptoms was an effect modifier. Both patients presenting with stroke and patients presenting with transient ischemic attacks (TIA) or amaurosis fugax (AF) had increased

Corresponding author: Mahmoud B. Malas, MD, MHS, RPVI, FACS, Professor in Residence, Chief, Division of Vascular and Endovascular Surgery, University of California San Diego, 9300 Campus Point Drive #7403, La Jolla, CA 92037-7403, Tel (858) 657-7404, Fax (858) 657-5033, mmalas@ucsd.edu.

risk of stroke/death when undergoing urgent compared to late TCAR: [OR:2.7, 95%CI:1.1–6.6, p=0.04] and [OR:4.1, 95%CI:1.1–15.0, p=0.03] respectively. However only patients presenting with TIA or AF had experienced increased risk of stroke when undergoing urgent compared to late TCAR: [OR:5.0, 95%CI:1.4–17.5, p<0.01]. At one-year follow-up, no differences were seen in recurrent ipsilateral stroke (urgent:0.7%, early:0.2%, late:0.1%, p=0.13) or post-discharge mortality (urgent:0.7%, early:1.6%, late:1.8%, p=0.71).

Conclusion: TCAR has a reduced incidence of stroke when performed 48-hours after onset of symptoms. Urgent TCAR within 48 hours of onset of stroke is associated with a three-fold increased risk of in-hospital stroke/death with no added benefit up to one year after the intervention. Further studies are needed on long-term outcomes of TCAR stratified by timing of the procedure.

Table of Contents Summary:

This VQI analysis of 2,608 symptomatic TCAR patients demonstrates increased risks associated with TCAR performed within 48-hours of onset of symptoms. The authors suggest delaying TCAR to at least 48-hours after onset of symptoms.

Keywords

timing; urgent; transCarotid artery revascularization; TCAR; flow reversal

Introduction

Surgical intervention has demonstrated superior long-term outcomes compared to medical management for symptomatic carotid artery stenosis[1]. Delays in intervention may result in recurrent stroke, which can reach 11% in the first 72-hours after the onset of symptoms[2,3]. This risk is greatest among patients presenting with stroke and lowest among patients presenting with amaurosis fugax (AF)[4,5]. Early intervention is intended to protect against early neurologic events but may also offer long-term benefit. In a pooled analysis of the North American Symptomatic Carotid Artery Trial and European Symptomatic Carotid Surgery Trial, patients receiving revascularization within two weeks of symptoms had the greatest absolute risk reduction in five-year recurrent ischemic stroke risk[6]. These studies suggest that earlier intervention decreases risk of recurrent stroke and results in improved patient outcomes[4,7–9]. The natural history of atherosclerotic disease, however, must be balanced against perioperative risks.

Recently symptomatic lesions are associated with higher perioperative risk of stroke. In a prospective study of the national Swedish Vascular Registry, patients operated on within 48 hours of AF, transient ischemic attacks (TIA), crescendo TIA, minor stroke, or major stroke had a 4-fold increased risk of perioperative stroke or death[5]. Urgent intervention may have increased risk due to manipulation of an unstable plaque facilitating embolization. Recently ischemic brain penumbra is also vulnerable to intraoperative hemodynamic and perfusion changes[10] which is susceptible to intra-operative neurological damage. Outside of this acute window, perioperative stroke and mortality were comparable between patients receiving intervention within 14-days of symptoms versus patients delaying intervention to 14-days

after symptoms[11–15]. Current recommendations from Society of Vascular Surgery's recommends intervention within two weeks of index symptoms[16].

The recommendations on timing of carotid revascularization focus on carotid endarterectomy (CEA). Studies on optimal timing of transfemoral carotid artery stenting (TFCAS) mimic trends seen in CEA, with increased risk associated with TFCAS performed within seven days after symptoms[17]. However, TFCAS has greater overall risks of perioperative complications than CEA[18,19] and this risk difference is greatest when revascularization is performed within the first week after presentation[20]. Therefore, CEA remains the gold standard for early revascularization.

TransCarotid Artery Revascularization (TCAR) is a novel stenting technique that avoids the aortic arch and utilizes intraoperative dynamic flow reversal to carry emboli away from the brain[21]. TCAR offers an attractive alternative for TFCAS[19,22] and CEA[23] with stroke rates as low as 1.4%[24] and promising mid-term patency results[25]. TCAR has also demonstrated safety in patients with high risk anatomic or physiologic factors[26,27]. To date, there are no studies on postoperative outcomes of TCAR stratified by timing of the procedure. Thus, the purpose of this study is to assess in-hospital rates of stroke, death, and MI, as well as one-year ipsilateral stroke and death among patients undergoing TCAR during different time intervals following the onset of symptoms.

Methods

We performed a retrospective analysis of the Society for Vascular Surgery (SVS) Vascular Quality Initiative (VQI) CAS registry. TCAR procedures performed since the start of the TCAR Surveillance Project (September 2016) to November 2019 were included. Patients excluded from this analysis include patients receiving intervention from a transfemoral, brachial, or radial approach, patients receiving TCAR for non-atherosclerotic lesions, patients receiving CAS for more than one lesion, and patients undergoing concomitant procedures. Patients were divided into the following groups:

1. Patients receiving urgent TCAR: between 0–2 days from the most recent symptom
2. Patients receiving early TCAR: between 3–14 days from the most recent symptom
3. Patients receiving late TCAR: between 15 and 180 days from the most recent symptom.

Only deidentified information from participating institutions in VQI was used for this analysis, therefore the need for Institutional Review Board and informed consent is waived for this study.

Outcomes

The primary outcome of interest was in-hospital stroke or death. Secondary outcomes of interest include in-hospital stroke, in-hospital death, in-hospital TIA, in-hospital stroke or TIA, in-hospital stroke, death or myocardial infarction (MI), non-home discharge and

recurrent ipsilateral ischemic stroke or death at one-year follow-up. Non-home discharge was defined as any patient who did not come from a nursing home and was discharged to a nursing home, rehabilitation facility, or other hospital. Stroke was defined as permanent neurologic symptoms that could include, full or partial visual loss, motor/sensory loss, speech abnormality, other new neurologic symptoms related to the right or left hemisphere, or symptom that are bilateral motor, sensory, or visual loss, diplopia, ataxia. TIA was defined as any focal neurologic deficit that resolved within twenty-four hours. MI is defined as sustained troponin increase, based on EKG findings, or based on clinical findings.

Statistical Analysis

Categorical baseline characteristics across the three groups were compared using Pearson $\chi 2$ test or Fisher exact test; continuous variables were compared using Analysis of Variance (ANOVA). Multivariable logistic regression analysis was used to calculate the odds ratios (OR) comparing urgent intervention to late intervention and early intervention to late intervention. Late intervention was chosen as the reference group since most patients underwent late TCAR. Kaplan Meier survival analysis was used to calculate the hazards ratio (HR) comparing urgent intervention to late intervention and early intervention to late intervention. Initial univariate analysis included the following predictors: age, sex, race, ethnicity, presentation type (stroke versus TIA/AF), body mass index (BMI), hypertension, diabetes, coronary artery disease (CAD), congestive heart failure (CHF), prior coronary intervention, chronic obstructive pulmonary disease (COPD), hemodialysis, smoking status, American Society of Anesthesiologists (ASA) classification, degree of stenosis, contralateral occlusion, prior ipsilateral carotid intervention, use of general anesthesia and preoperative medications, including aspirin, P2Y12 receptor antagonists, anticoagulants, beta blockers, angiotensin converting enzyme (ACE) inhibitors, and statins. Stepwise backward and forward selection was then performed, and covariates were chosen based on Akaike's Information Criterion (AIC). The model with the lowest AIC value is deemed the most parsimonious and informative in predicting the outcome of interest[28]. All analyses were clustered by centers to account for intragroup correlation and all appropriate theory-based categorical-categorical interactions were tested for and those that were found significant were presented. Hosmer-Lemeshow tests were used to assess the discrimination and calibration of the models[29]. The final model included: race, age, CAD, CHF, diabetes, COPD, presentation with stroke versus TIA, use of general anesthesia, and pre-operative P2Y12. Presentation type was found to be an effect modifier and analysis was repeated in subgroups based on presentation. All calculations were completed using R version 3.6.2. A p-value <0.05 was considered statistically significant.

Results

A total of 2608 patients were included: 144 urgent (5.52%), 928 early (35.58%), and 1536 (58.90%) late. Patients undergoing urgent intervention were less likely to be white (8.3% urgent, 13.8% early, 9.3% late, $p<0.01$), current smokers (45.1% urgent, 42.8% early, 51.8% late, $p<0.001$), to have CAD (38.9% urgent, 41.8% early, 46.4% late, $p=0.03$), to have COPD (17.2% urgent, 26.9% early, 32.8% late, $p<0.001$), to be taking P2Y12 inhibitors (74.3% urgent, 84.1% early, 90.2% late, $p<0.001$) and statins (81.9% urgent, 89.8% early,

91.3% late, p<0.01), to present with stroke (49.3% urgent, 56.9% early, 50.7% late, p=0.01). Patients undergoing early intervention were less likely to undergo general anesthesia (81.2% urgent, 76.5% early, 81.6% late, p<0.01) (Table I). All adjusted models had non-significant Hosmer-Lemeshow p-values and C-statistics>0.5.

Analysis of all patients regardless of presenting symptoms :

There was increased risk of stroke (urgent: 5.6%, early: 2.5%, late: 2.0%, p=0.03), TIA (urgent: 3.5%, early: 1.1%, late: 0.8%, p=0.02) and stroke/TIA (urgent: 8.3%, early: 3.6%, late: 2.7%, p=0.004) in urgent compared to early and late interventions. This contributed to significant differences in composite stroke/death (urgent: 6.5%, early: 2.9%, late: 2.3%, p=0.02) but there were no differences in composite stroke/death/MI rates (urgent: 6.5%, early: 3.2%, late: 2.8%, p=0.08). There were also no differences in rates of in-hospital death (urgent: 1.4%, early: 1.0%, late: 0.5%, p-value=0.12). After adjusting for potential confounders, urgent intervention had more than 2-folds increased odds of stroke [OR:2.8, 95%CI:1.3–6.2, p=0.01], which drove increased odds of stroke/death and stroke/death/MI when compared to late intervention [OR:2.9, 95%CI:1.3–6.4, p=0.01] and [OR: 2.4, 95%CI: 1.1–5.1, p=0.02], respectively. There were no differences comparing early to late intervention in the odds of stroke/death and stroke/death/MI, [OR:1.2, 95%CI:0.7–2.1, p=0.48] and [OR:1.1, 95%CI:0.7–1.8, p=0.67] respectively.

Both urgent and early intervention groups had increased risk of non-home discharges (urgent: 23.6%, early: 22.3%, late: 6.6%, p<0.001). These differences persisted after adjusting with 4-fold increased odd of non-home discharge in urgent and early compared to late interventions [Urgent OR: 4.9, 95%CI:3.3–7.2, p<0.001], [Early OR: 4.2, 95%CI:3.2–5.5, p<0.001] (Table II).

At one-year follow-up, there were no differences in late mortality rates after discharge among the urgent (0.7%), early (1.6%) and late (1.8%) cohorts (p=0.71): urgent versus late [HR:1.1, 95%CI:0.6–2.0, p=0.33]; early versus late [HR:0.4, 95%CI:0.1–2.7, p=0.85]. Recurrent ipsilateral stroke rates were also comparable across urgent (0.7%), early (0.2%), and late (0.1%) cohorts (p=0.57): urgent versus late [HR:10.7, 95%CI:0.4–43.4, p=0.10]; early versus late [HR:10.1, 95%CI:0.6–164.7, p=0.26] (Table III, Figure Ia, Figure Ib).

Analysis of patients presenting with Stroke:

Rates of stroke (urgent: 5.6%, early: 2.5%, late: 2.6%; p=0.26) and stroke/death (urgent: 5.6%, early: 3.1%, late: 2.8%, p=0.11) were comparable between the three timing intervals. However, the rates of stroke/TIA were significantly higher in the urgent group (urgent: 9.9%, early: 3.6%, late: 3.2%, p=0.03). This persisted on adjusted analysis [urgent compared to late OR:2.9 95%CI:1.0–7.9, p=0.04] [early compared to late OR:1.1 95%CI:0.6–2.2, p=0.75]. Furthermore, odds of stroke/death were significantly higher in the urgent cohort but not the early cohort compared to the late cohort on adjusted analysis [OR:2.7, 95%CI:1.1–6.6, p=0.04] and [OR:1.1, 95%CI:0.6–2.2, p=0.75], respectively. Rates of non-home discharge (urgent: 33.8%, early: 31.9%, late: 9.9%, p<0.001) were also significantly different, even after adjusting for urgent compared to late [OR:4.8, 95%CI:2.9–7.9,

p<0.001], and early compared to late [OR:4.6, 95%CI:3.3–6.5, p<0.001] (Supplementary Table Ia).

Analysis of patients presenting with TIA or AF:

There were significant differences for patients presenting with TIA or AF in the risk of stroke depending on timing of operation (urgent: 5.5%, early: 2.5%, late: 1.3%, p=0.03). These differences persisted on adjusted analysis in urgent but not early compared to late odds stroke [OR:5.0, 95%CI:1.4–17.6, p=0.01], which contributed to increased odds of stroke/TIA [OR:3.7, 95%CI: 1.1–11.9, p=0.03] and stroke/death [OR:4.1, 95%CI:1.1–15.0, p=0.03] in the urgent group. Rates of non-home discharge were also significantly higher in urgent and early TCAR (urgent: 13.7%, early: 9.8%, late: 3.2%, p-value<0.001) on adjusted analysis (urgent versus late [OR:5.6, 95%CI:2.4–13.1, p<0.001], early versus late [OR:3.1, 95%CI:1.8–5.2, p<0.001]) (Supplementary Table Ib).

Discussion

This study evaluated the effects of timing on in-hospital and midterm outcomes after TCAR among 2,608 symptomatic patients captured in VQI between September 2016 and November 2019. Urgent TCAR within 48-hours of symptoms demonstrated three-fold increased odds of stroke/death, which was driven primarily by greater odds of stroke. Early TCAR performed between 3–14 days after symptoms is preferable as these patients had a similar rate of stroke/death compared to late TCAR and only demonstrated increased odds of non-home discharge. These results persist after adjustment for potential confounders such as coronary artery disease and preoperative medications. Type of symptoms at presentation was an effect modifier. At one-year follow-up, urgent or early intervention did not confer long-term stroke or mortality benefit.

Plaque morphology and evolution may contribute to intraoperative embolization in urgent intervention. Certain carotid plaque characteristics, such as inflammation, intraplaque hemorrhage, lipid core, and thinning or rupture of a fibrous cap, are known markers of plaque instability as they are associated with increased risk of initial and recurrent stroke[30,31]. After stroke, carotid plaques experience a gradual decrease in inflammatory cytokines, decrease in concentrations of macrophages and increase in percentage of smooth muscle cells out to six months after symptoms[32]. The Oxford Plaque study also found that plaques isolated from endarterectomy performed sooner after symptoms had more of these unstable histologic markers, including decreased smooth muscle cells and increased macrophages[33]. These findings suggest that plaques become more stable over time, which may contribute to increased risk with intraoperative manipulation of the plaque during urgent or early interventions.

Intra-operative embolization risk is especially high during stent placement. In a study utilizing intra-operative transcranial doppler imaging, both TCAR and TFCAS had a peak in embolization during the protection phase[34]. These findings suggest that stent deployment disturbs the plaque, although TCAR with flow reversal had significantly decreased number and duration of embolization compared to TFCAS with distal embolic protection devices (p<0.001 for both)[35]. These results suggest that intra-operative embolization risk is largely

minimized during TCAR when compared to TFCAS. While data on timing of post-operative strokes is available in VQI, more than 10% of eligible patients (9/70) had missing data and this endpoint was therefore excluded from our analysis. It is possible that the unstable nature of recently symptomatic plaques causes further embolization after the flow reversal ended as the stent continues to expand in the postoperative period. Moreover, literature has suggested that TCAR can tolerate other embolic inducing maneuvers, such as with post-stent ballooning. For example, prior studies from our group have found that post-stent dilation is associated with almost double the risk of postoperative ballooning when compared to pre-stent dilation among patients undergoing transfemoral stenting[36]. More recently, we have found that the timing of ballooning is less impactful on TCAR outcomes, likely due to the superiority of flow-reversal over distal embolic devices[37]. Despite the lack of clinical data on timing of post-operative strokes among TCAR, this literature suggests that the increased odds of stroke in the urgent cohort is more likely attributed to post-operative embolization risks.

Post-operative embolization may contribute to higher risks during the urgent group. TCAR requires high intra-operative systolic blood pressure up to 160 mmHg to ensure continued cerebral perfusion during flow reversal. Hemodynamic status is strictly monitored and maintained through intraoperative administration of glycopyrrolate and/or phenylephrine. Stents continue to expand postoperatively which may increase the risk of embolization especially in unstable vulnerable plaque[38]. Patients might experience hemodynamic depression due to stent expansion with decrease in blood pressure post-operatively. This is less tolerated by the ischemic penumbra in the early days after stroke.

Early literature studying urgent revascularization also noted an increased risk of hemorrhagic conversion due to acute reperfusion syndrome[39–41]. This risk may be compounded by the increasing utilization of dual antiplatelet therapy[42,43]. While not all subsequent literature has supported cerebral hyperperfusion syndrome associated with urgent carotid revascularization, further studies are needed to evaluate the impact of dual antiplatelet therapy on hemorrhagic risk.

It is also possible that urgent TCAR is safe for a smaller subset of patients with favorable characteristics. Some TFCAS timing studies have noted no difference in outcomes when performing stenting in the acute 48-hour period with strict inclusion criteria, such as exclusion of patients with low-grade stenosis with ulcerated plaques[17]. Other studies have cited strict perioperative antiplatelet initiation[44] and tight interdisciplinary collaboration to offer 24/7 interventions[45], as key components to safe urgent intervention.

In our analysis, the type of symptoms on presentation was an effect modifier of the postoperative outcomes. Patients presenting with TIA or AF had higher rates of postoperative neurologic complications, including stroke and stroke/TIA. Patients presenting with stroke had higher rates of postoperative stroke/death although postoperative stroke and postoperative death risks were not independently higher. These results contrast with other studies on stroke risk stratified by presentation type. Traditionally, patients presenting with stroke have higher perioperative risk of stroke than patients presenting with TIA or AF[46]. The small population of urgent patients in each subgroup of our study may have contributed

to a type II statistical error. A clinical explanation may also be possible: patients presenting with stroke have dislodged unstable portions of the plaque and embolization risk from the remnants are low. While risk of stroke is independently not significant, risk of stroke combined with risk of death may be significantly higher in the urgent cohort. Lesions presenting with TIA may be embolizing small pieces, leaving most of the unstable plaque intact and likely to embolize. There is limited scientific evidence for this hypothesis, however a study on emergent CEA using the American College of Surgeons National Surgical Quality Improvement Program found similar findings[47]. Patients presenting with TIA undergoing emergent CEA experienced increased risk of stroke ($p<0.001$), stroke/death ($p<0.001$), and stroke/death/MI ($p=0.002$) but patients presenting with stroke undergoing emergent CEA only experienced increased risk of stroke/death/MI ($p=0.026$).

Despite the increased risk associated with urgent TCAR, the stroke rate of 5.6% in the urgent group is less than other retrospective studies looking at urgent revascularization among carotid endarterectomy patients, including 8.2% in the Southern California database[48] and 11% in the Swedish National Vascular Registry[5]. The stroke rate of 2.5% among early patients is comparable to overall CEA risk. While this study did not directly compare TCAR to CEA, these results are promising. Further clinical trials conducted in both academic and community hospitals are needed to better understand whether TCAR can be safely performed within the two weeks window recommended by the Society of Vascular Surgery guidelines[49]. Our study also found no difference in one-year survival or recurrent stroke, although there was a trend towards decreased mortality among urgent and early interventions. These findings contrast the conclusions from compiled North American Carotid Stenting Trial and European Carotid Surgery Trial data, which found five-year survival benefit with earlier interventions[6]. Our analysis may be subject to selection bias, as one-third of all patients and half of patients eligible for follow-up (728 of 1358 (53.61%) cases performed prior to November 2018) have data at one-year, as well as type II statistical error, since only forty patients in the urgent cohort had one-year data. As this cohort ages, more follow-up should become available and this analysis may be repeated. In addition, the low event rates are more suitable for five-year or ten-year survival or mortality. Therefore, conclusions cannot be drawn regarding the long-term efficacy and clinical outcomes of urgent or early intervention.

While these results appear to be compelling, we cannot underestimate the risk of selection bias. Patients who underwent urgent operation may have been at the highest risk for recurrent strokes. There is no way to evaluate whether patients in the early or late group may have suffered a more adverse outcome by deferring the time to intervention. Another limitation is the potential heterogeneity of stroke patients in regard of the severity of symptoms. Further studies are needed to apply a severity index such as the NIH Stroke Scale or Rankin scale. Finally, there is a lack of consistent and granular data on timing of post-operative stroke. VQI only provides data on whether strokes occurred intraoperatively, within six hours after the procedure, or more than six hours after the procedure. Of the patients who experienced postoperative stroke, more than 10% had missing data. Complete and granular data on timing of post-operative stroke would better elucidate the pathophysiology behind our findings.

There are other limitations to a multi-institutional database, including coding errors, incomplete data, and other systematic biases. However, the Vascular Quality Initiative has been studied rigorously and used in over 200 peer-reviewed studies. These limitations are being addressed by the SPREAD-STACI trial randomizing patients to urgent and early intervention[50], however results has not yet been published.

Conclusion

TCAR is safest in symptomatic patients when performed at least three-days after symptoms. TCAR performed within 48-hours had three-fold increased risk of postoperative stroke or death. There is no preventative or survival benefit at one-year associated with urgent or early intervention, although analysis was limited by low rates of follow-up. As the TSP continues with increased number of patients and longer follow up, further analysis will be planned. Larger studies with longer follow up are needed to confirm the findings of this study.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

This study was accepted at the 2020 Vascular Annual Meeting of the Society for Vascular Surgery, Toronto, Canada.

Type of Research: Retrospective review of prospectively collected Vascular Quality Initiative data.

Key Findings: Of 2,608 TCAR procedures performed for symptomatic patients between September 2016 and November 2019, patients underwent intervention at the following time points after symptoms [5% within 48-hours, 36% at 3–14 days, and 59% at >2 weeks]. Patients undergoing 48-hour intervention had three-fold increased odds of in-hospital stroke/death, driven by increased odds of stroke.

Take Home Message: TCAR within 48-hours of symptoms had increased risk of in-hospital complications.

References

1. Rothwell PM, Eliasziw M, Gutnikov SA, Fox AJ, Taylor DW, Mayberg MR, et al. Analysis of pooled data from the randomised controlled trials of endarterectomy for symptomatic carotid stenosis. Lancet. 2003;361(9352):107–116. [PubMed: 12531577]
2. Lovett JK, Coull AJ, Rothwell PM. Early risk of recurrence by subtype of ischemic stroke in population-based incidence studies. Neurology. 2004;62(4):569–573. [PubMed: 14981172]
3. Mono ML, Steiger I, Findling O, Jung S, Reinert M, Galimanis A, et al. Risk of very early recurrent cerebrovascular events in symptomatic carotid artery stenosis. J Neurosurg. 2013;119(6): 1620–1626. [PubMed: 23971962]
4. Johansson EP, Arnerlov C, Wester P. Risk of recurrent stroke before carotid endarterectomy: the ANSYSCAP study. Int J Stroke. 2013;8(4):220–227. [PubMed: 22494778]
5. Stromberg S, Gelin J, Osterberg T, Bergstrom GM, Karlstrom L, Osterberg K, et al. Very urgent carotid endarterectomy confers increased procedural risk. Stroke. 2012;43(5): 1331–1335. [PubMed: 22426315]
6. Rothwell PM, Eliasziw M, Gutnikov SA, Warlow CP, Barnett HJM. Endarterectomy for symptomatic carotid stenosis in relation to clinical subgroups and timing of surgery. The Lancet. 2004;363(9413):915–924.

7. Marnane M, Ni Chroinin D, Callaly E, Sheehan OC, Merwick A, Hannon N, et al. Stroke recurrence within the time window recommended for carotid endarterectomy. Neurology. 2011;77(8):738–743. [PubMed: 21849640]
8. Johansson E, Cuadrado-Godia E, Hayden D, Bjellerup J, Ois A, Roquer J, et al. Recurrent stroke in symptomatic carotid stenosis awaiting revascularization: A pooled analysis. Neurology. 2016;86(6):498–504. [PubMed: 26747885]
9. Kjorstad KE, Baksaas ST, Bundgaard D, Halbakken E, Hasselgard T, Jonung T, et al. Editor's Choice - The National Norwegian Carotid Study: Time from Symptom Onset to Surgery is too Long, Resulting in Additional Neurological Events. Eur J Vasc Endovasc Surg. 2017; 54(4) :415–422. [PubMed: 28844552]
10. Biller J, Feinberg WM, Castaldo JE, Whittemore AD, Harbaugh RE, Dempsey RJ, et al. Guidelines for carotid endarterectomy: a statement for healthcare professionals from a special writing group of the Stroke Council, American Heart Association. Stroke. 1998;29(2):554–562. [PubMed: 9480580]
11. Huang Y, Gloviczki P, Duncan AA, Kalra M, Oderich GS, DeMartino RR, et al. Outcomes after early and delayed carotid endarterectomy in patients with symptomatic carotid artery stenosis. J Vasc Surg. 2018;67(4): 1110–1119 e1111. [PubMed: 29224943]
12. Ballotta E, Meneghetti G, Da Giau G, Manara R, Saladini M, Baracchini C. Carotid endarterectomy within 2 weeks of minor ischemic stroke: a prospective study. J Vasc Surg. 2008;48(3):595–600. [PubMed: 18585887]
13. Meschia JF, Hopkins LN, Altafullah I, Wechsler ER, Stotts G, Gonzales NR, et al. Time From Symptoms to Carotid Endarterectomy or Stenting and Perioperative Risk. Stroke. 2015;46(12):3540–3542. [PubMed: 26493675]
14. Brinjikji W, Rabinstein AA, Meyer FB, Piepgras DG, Eanzino G. Risk of early carotid endarterectomy for symptomatic carotid stenosis. Stroke. 2010;41(10):2186–2190. [PubMed: 20798367]
15. Salem MK, Sayers RD, Bown MJ, Eveson DJ, Robinson TG, Naylor AR. Rapid access carotid endarterectomy can be performed in the hyperacute period without a significant increase in procedural risks. Eur J Vasc Endovasc Surg. 2011;41(2):222–228. [PubMed: 21130006]
16. Ricotta JJ, Aburahma A, Ascher E, Eskandari M, Faries P, Lal BK, et al. Updated Society for Vascular Surgery guidelines for management of extracranial carotid disease. Journal of vascular surgery. 2011;54(3):e1–e31. [PubMed: 21889701]
17. Tsantilas P, Kuehnl A, Kallmayer M, Knappich C, Schmid S, Breitkreuz T, et al. Risk of Stroke or Death Is Associated With the Timing of Carotid Artery Stenting for Symptomatic Carotid Stenosis: A Secondary Data Analysis of the German Statutory Quality Assurance Database. J Am Heart Assoc. 2018;7(7).
18. Murad MH, Shahrour A, Shah ND, Montori VM, Ricotta JJ. A systematic review and meta-analysis of randomized trials of carotid endarterectomy vs stenting. J Vasc Surg. 2011; 53(3):792–797. [PubMed: 21216556]
19. Malas MB, Dakour-Aridi H, Wang GJ, Kashyap VS, Motaganahalli RL, Eldrup-Jorgensen J, et al. Transcarotid artery revascularization versus transfemoral carotid artery stenting in the Society for Vascular Surgery Vascular Quality Initiative. J Vasc Surg. 2019;69(1):92–103 e102. [PubMed: 29941316]
20. Rantner B, Goebel G, Bonati LH, Ringleb PA, Mas JL, Fraedrich G, et al. The risk of carotid artery stenting compared with carotid endarterectomy is greatest in patients treated within 7 days of symptoms. J Vasc Surg. 2013;57(3):619–626 e612; discussion 625–616. [PubMed: 23237679]
21. Malas MB, Leal J, Kashyap V, Cambria RP, Kwolek CJ, Criado E. Technical aspects of transcarotid artery revascularization using the ENROUTE transcarotid neuroprotection and stent system. J Vasc Surg. 2017;65(3):916–920. [PubMed: 28236931]
22. Schermerhorn ML, Liang P, Eldrup-Jorgensen J, Cronenwett JL, Nolan BW, Kashyap VS, et al. Association of Transcarotid Artery Revascularization vs Transfemoral Carotid Artery Stenting With Stroke or Death Among Patients With Carotid Artery Stenosis. JAMA. 2019;322(23):2313–2322. [PubMed: 31846015]

23. Schermerhorn ML, Liang P, Dakour-Aridi H, Kashyap VS, Wang GJ, Nolan BW, et al. In-hospital outcomes of transcarotid artery revascularization and carotid endarterectomy in the Society for Vascular Surgery Vascular Quality Initiative. J Vasc Surg. 2020;71(1):87–95. [PubMed: 31227410]
24. Kwolek CJ, Jaff MR, Leal JI, Hopkins LN, Shah RM, Hanover TM, et al. Results of the ROADSTER multicenter trial of transcarotid stenting with dynamic flow reversal. J Vasc Surg. 2015;62(5):1227–1234. [PubMed: 26506270]
25. Malas MB, Leal Lorenzo JI, Nejim B, Hanover TM, Mehta M, Kashyap V, et al. Analysis of the ROADSTER pivotal and extended-access cohorts shows excellent 1-year durability of transcarotid stenting with dynamic flow reversal. J Vasc Surg. 2019;69(6):1786–1796. [PubMed: 30611582]
26. Kashyap VS, King AH, Foteh MI, Janko M, Jim J, Motaganahalli RL, et al. A multi-institutional analysis of transcarotid artery revascularization compared to carotid endarterectomy. J Vasc Surg. 2019;70(1):123–129. [PubMed: 30622007]
27. Wu WW, Liang P, O'Donnell TFX, Swerdlow NJ, Li C, Wyers MC, et al. Anatomic eligibility for transcarotid artery revascularization and transfemoral carotid artery stenting. J Vasc Surg. 2019;69(5):1452–1460. [PubMed: 30853384]
28. Bozdogan H Model selection and Akaike's Information Criterion (AIC): The general theory and its analytical extensions. Psychometrika. 1987;52:345–370.
29. Lemeshow S, Hosmer DW Jr. A review of goodness of fit statistics for use in the development of logistic regression models. Am J Epidemiol. 1982;115(1):92–106. [PubMed: 7055134]
30. Deng F, Mu C, Yang L, Li H, Xiang X, Li K, et al. Carotid plaque magnetic resonance imaging and recurrent stroke risk: A systematic review and meta-analysis. Medicine (Baltimore). 2020;99(13):el9377.
31. Selwaness M, Bos D, van den Bouwhuijsen Q, Portegies ML, Ikram MA, Hofman A, et al. Carotid Atherosclerotic Plaque Characteristics on Magnetic Resonance Imaging Relate With History of Stroke and Coronary Heart Disease. Stroke. 2016;47(6):1542–1547. [PubMed: 27165952]
32. Peeters W, Hellings WE, de Kleijn DP, de Vries JP, Moll FL, Vink A, et al. Carotid atherosclerotic plaques stabilize after stroke: insights into the natural process of atherosclerotic plaque stabilization. Arterioscler Thromb Vasc Biol. 2009;29(1):128–133. [PubMed: 18931283]
33. Redgrave JN, Lovett JK, Gallagher PJ, Rothwell PM. Histological assessment of 526 symptomatic carotid plaques in relation to the nature and timing of ischemic symptoms: the Oxford plaque study. Circulation. 2006;113(19):2320–2328. [PubMed: 16651471]
34. Plessers M, Van Herzeele I, Hemelsoet D, Patel N, Chung EM, Vingerhoets G, et al. Transcervical Carotid Stenting With Dynamic Flow Reversal Demonstrates Embolization Rates Comparable to Carotid Endarterectomy. JEndovasc Ther. 2016;23(2):249–254. [PubMed: 26794908]
35. Fairman R, Gray WA, Scicli AP, Wilburn O, Verta P, Atkinson R, et al. The CAPTURE registry: analysis of strokes resulting from carotid artery stenting in the post approval setting: timing, location, severity, and type. Ann Surg. 2007;246(4):551–556; discussion 556–558. [PubMed: 17893491]
36. Obeid T, Arnaoutakis DJ, Arhuidese I, Qazi U, Abularrage CJ, Black J, et al. Poststent ballooning is associated with increased periprocedural stroke and death rate in carotid artery stenting. J Vasc Surg. 2015;62(3):616–623 e611. [PubMed: 26033011]
37. Malas MB, Dakour-Aridi H, Barleben A, Nolan B, Schermerhorn ML, Jorgensen J. Outcomes of Post-stent Ballooning After Transcarotid Artery Revascularization (TCAR) (Abstract). In "Western Vascular Society 2019 Annual Meeting Conference Proceedings".
38. Qazi U, Obeid T, Arhuidese I, Malas M. Carotid Artery Stent Continued Expansion Days After Deployment, Without Post Stent Deployment Angioplasty. Clin Pract. 2015;5(3):767. [PubMed: 26664713]
39. Moulakakis KG, Mylonas SN, Sfyroeras GS, Andrikopoulos V. Hyperperfusion syndrome after carotid revascularization. J Vasc Surg. 2009;49(4):1060–1068. [PubMed: 19249185]
40. Noorani A, Sadat U, Gaunt ME. Cerebral hemodynamic changes following carotid endarterectomy: 'cerebral hyperperfusion syndrome'. Expert Rev Neurother. 2010;10(2):217–223. [PubMed: 20136378]

41. Kirchoff-Torres KF, Bakradze E. Cerebral Hyperperfusion Syndrome After Carotid Revascularization and Acute Ischemic Stroke. Curr Pain Headache Rep. 2018;22(4):24. [PubMed: 29556806]

42. Dalainas I, Nano G, Bianchi P, Stegher S, Malacrida G, Tealdi DG. Dual antiplatelet regime versus acetyl-acetic acid for carotid artery stenting. Cardiovasc Intervent Radiol. 2006;29(4): 519–521. [PubMed: 16565792]

43. McKevitt FM, Randall MS, Cleveland TJ, Gaines PA, Tan KT, Venables GS. The benefits of combined anti-platelet treatment in carotid artery stenting. Eur J Vasc Endovasc Surg. 2005;29(5):522–527. [PubMed: 15966092]

44. Sharpe R, Sayers RD, London NJ, Bown MJ, McCarthy MJ, Nasim A, et al. Procedural risk following carotid endarterectomy in the hyperacute period after onset of symptoms. Eur J Vasc Endovasc Surg. 2013;46(5):519–524. [PubMed: 24074894]

45. Rantner B, Schmidauer C, Knoflach M, Fraedrich G. Very urgent carotid endarterectomy does not increase the procedural risk. Eur J Vasc Endovasc Surg. 2015;49(2):129–136. [PubMed: 25445726]

46. Geraghty PJ, Brothers TE, Gillespie DL, Upchurch GR, Stoner MC, Siami FS, et al. Preoperative symptom type influences the 30-day perioperative outcomes of carotid endarterectomy and carotid stenting in the Society for Vascular Surgery Vascular Registry. J Vasc Surg. 2014;60(3):639–644. [PubMed: 25154963]

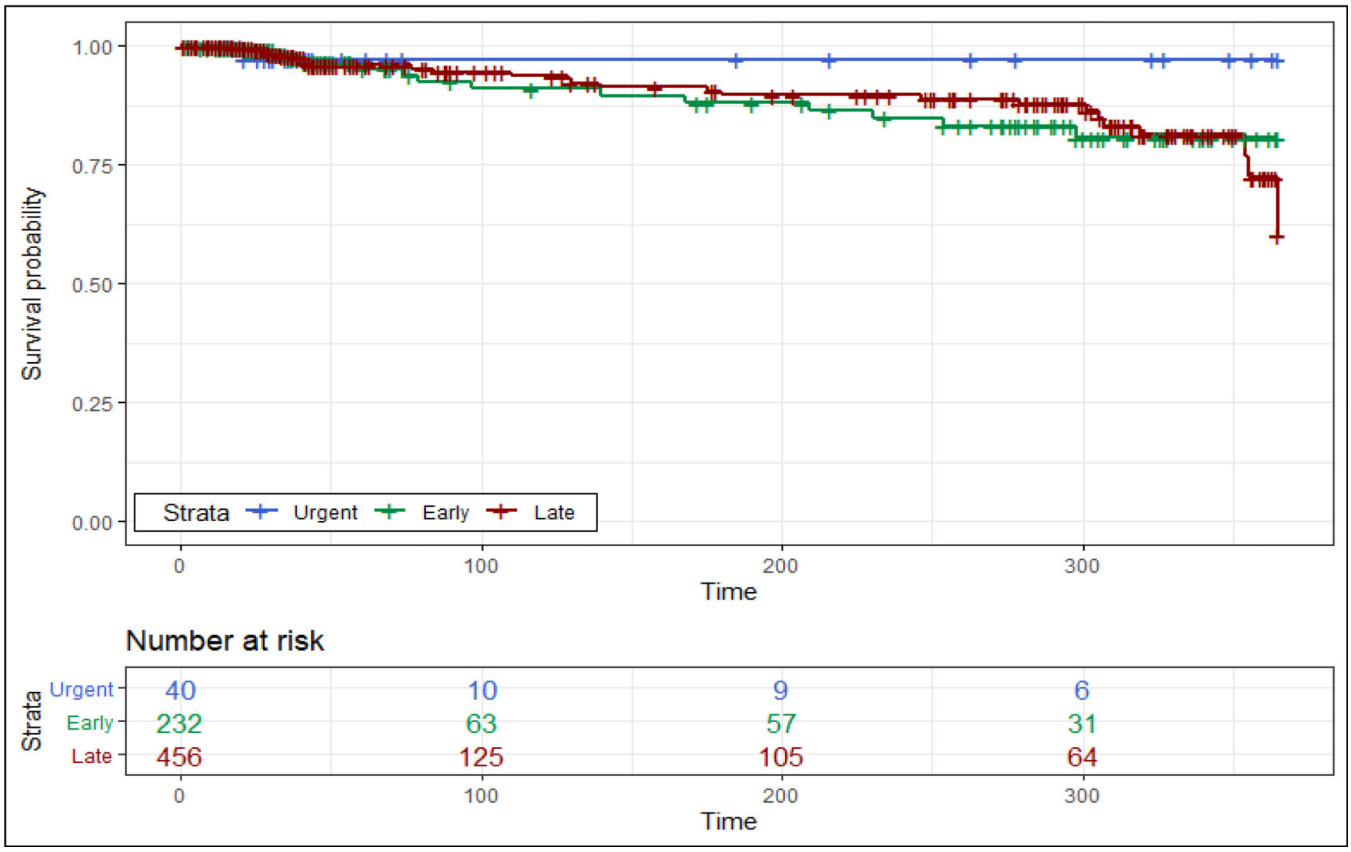
47. Faateh M, Dakour-Aridi H, Kuo PL, Locham S, Rizwan M, Malas MB. Risk of emergent carotid endarterectomy varies by type of presenting symptoms. J Vasc Surg. 2019;70(1):130–137 e131. [PubMed: 30777684]

48. Andersen JC, Mannoia KA, Kiang SC, Patel ST, Teruya TH, Bianchi C, et al. Immediate Carotid Endarterectomy Is Associated with Higher Risk in Symptomatic Patients. Ann Vasc Surg. 2019.

49. Ricotta JJ, Aburahma A, Ascher E, Eskandari M, Faries P, Lal BK, et al. Updated Society for Vascular Surgery guidelines for management of extracranial carotid disease. J Vasc Surg. 2011;54(3):e1–31. [PubMed: 21889701]

50. Lanza G, Ricci S, Speziale F, Toni D, Sbarigia E, Setacci C, et al. SPREAD-STACI study: a protocol for a randomized multicenter clinical trial comparing urgent with delayed endarterectomy in symptomatic carotid artery stenosis. Int J Stroke. 2012;7(1):81–85. [PubMed: 22151469]

a:



b:

Figure I.

a: One-year survival was not significantly different between the three timing cohorts (p=0.13).

b: One-year recurrent ipsilateral stroke rates were not significantly different between the three timing cohorts (p=0.71)

Table I.

Demographic characteristics for the different timing cohorts.

	0–2 days (n=144, 5.52%)	3–14 days (n=928, 35.58%)	15–180 days (n=1536, 58.9%)	P-Value
Demographics				
Sex (Female)	54 (37.5)	351 (37.8)	544 (35.4)	0.47
Age	72.6 ± 10.1	73.2 ± 10.4	72.8 ± 9.8	0.62
Race (Non-White)	12 (8.3)	128 (13.8)	142 (9.3)	< 0.01
Ethnicity (Hispanic)	4 (2.8)	35 (3.8)	62 (4.1)	0.74
BMI	29.9 ± 6.0	28.3 ± 6.0	28.7 ± 8.1	0.63
Comorbidities				
Diabetes	57 (39.6)	362 (39.0)	612 (39.8)	0.92
Hypertension	128 (88.9)	838 (90.3)	1397 (91.0)	0.64
Congestive Heart Failure	25 (17.4)	168 (18.1)	258 (16.8)	0.71
Coronary Artery Disease	56 (38.9)	388 (41.8)	713 (46.4)	0.03
History of CABG or PCI	44 (30.8)	302 (32.5)	543 (35.4)	0.25
Chronic Obstructive Pulmonary Disease	22 (17.2)	222 (26.9)	456 (32.8)	< 0.001
Current Smoker	65 (45.1)	397 (42.8)	794 (51.8)	< 0.001
GFR<60	82 (57.8)	508 (55.8)	910 (60.6)	0.07
Dialysis	2 (1.4)	15 (1.6)	26 (1.7)	0.96
Prior Ipsilateral CAS/CEA	12 (8.3)	84 (9.1)	160 (10.4)	0.45
Preoperative Hemoglobin (g/dL)	13.0 ± 2.1	13.0 ± 2.1	13.1 ± 1.9	0.05
Preoperative Medications				
Aspirin	127 (88.2)	833 (89.9)	1417 (92.3)	0.06
Beta Blockers	76 (52.8)	498 (53.7)	856 (55.7)	0.53
Statin	118 (81.9)	833 (89.8)	1402 (91.3)	<0.01
P2Y12 Inhibitors	107 (74.3)	780 (84.1)	1386 (90.2)	< 0.001
ACE Inhibitors	68 (47.2)	445 (48.0)	791 (51.5)	0.18
Presentation (Stroke)	71 (49.3)	528 (56.9)	779 (50.7)	0.01
Stenosis > 80%	63 (45.0)	391 (42.4)	679 (44.6)	0.55
General Anesthesia	117 (81.2)	709 (76.5)	1254 (81.6)	< 0.01

Table II:

In-hospital unadjusted and adjusted analysis for all symptomatic patients included in this analysis. Patients undergoing urgent TCAR had increased odds of in-hospital complications when compared to late intervention.

	Urgent (n=144, 5.52%)					Early (n=928, 35.58%)					Late (n=1536, 58.9%)		Chi-Square
		Unadjusted		Adjusted			Unadjusted		Adjusted				
	n (%)	OR (95%CI)	P-Value	OR (95%CI)	P-Value	n (%)	OR (95%CI)	P-Value	OR (95%CI)	P-Value	n (%)	OR (95%CI)	P-Value
Stroke	8 (5.6)	3.0 (1.4, 6.2)	0.004	2.8 (1.3, 6.2)	0.01	23 (2.5)	1.3 (0.7, 2.2)	0.38	1.3 (0.7, 2.3)	0.40	30 (2.0)	Reference	0.03
TIA	5 (3.5)	4.6 (1.4, 15)	0.01	4.2 (1.1, 16.5)	0.04	10 (11)	1.4 (0.6, 3.3)	0.46	1.3 (0.6, 3)	0.49	12 (0.8)	Reference	0.02
Death	2 (14)	3.1 (0.6, 15.7)	0.17	3.4 (0.6, 19.3)	0.17	9 (10)	2.2 (0.9, 5.2)	0.09	1.7 (0.7, 4.7)	0.27	7 (0.5)	Reference	0.12
MI	1 (0.7)	1.0 (0.1, 7.9)	0.98	1.4 (0.2, 11.3)	0.77	3 (0.3)	0.4 (0.1, 1.6)	0.23	0.5 (0.1, 1.9)	0.33	11 (0.7)	Reference	0.38
Stroke/TIA	12 (8.3)	3.2 (1.6, 6.7)	0.002	3.0 (1.4, 6.7)	0.01	33 (3.6)	1.3 (0.8, 2.1)	0.27	1.3 (0.8, 2.1)	0.31	42 (2.7)	Reference	0.004
Stroke/Death	9 (6.5)	3.0 (1.4, 6.2)	0.004	2.9 (1.3, 6.4)	0.01	26 (2.9)	1.3 (0.8, 2.1)	0.34	1.2 (0.7, 2.1)	0.48	34 (2.3)	Reference	0.02
Stroke/ Death/MI	9 (6.5)	2.4 (1.2, 4.9)	0.02	2.4 (1.1, 5.1)	0.02	29 (3.2)	1.2 (0.7, 1.9)	0.55	1.1 (0.7, 1.8)	0.67	42 (2.8)	Reference	0.08
Cranial Nerve Injury	1 (0.7)	2.7 (0.3, 22.7)	0.37	2.6 (0.3, 23.3)	0.39	5 (0.5)	2.1 (0.5, 7.9)	0.28	2.4 (0.6, 8.8)	0.19	4 (0.3)	Reference	0.26
Non-home Discharge	34 (23.6)	4.4 (3.0, 6.3)	<0.001	4.9 (3.3, 7.2)	<0.001	207 (22.3)	4.1 (3.2, 5.3)	<0.001	4.2 (3.2, 5.5)	<0.001	101 (6.6)	Reference	<0.001

Table III:

One-year recurrent ipsilateral stroke and one-year mortality for all patients. No significant differences were seen.

	Urgent (n=40)			Early (n=232)			Late (n=456)		P-Value
	n (%)	HR (95% CI)	P-Value	n (%)	HR (95% CI)	P-Value	n (%)	HR (95% CI)	
Stroke	1 (0.7)	10.7 (0.4, 43.4)	0.10	2 (0.2)	10.1 (0.6, 164.7)	0.26	1 (0.1)	Reference	0.13
Death	1 (0.7)	1.1 (0.6, 2.0)	0.33	15 (1.6)	0.4 (0.1, 2.7)	0.85	28 (1.8)	Reference	0.71