Coexisting Coronary and Carotid Artery Disease – Which Technique and in Which Order? Case Report and Review of Literature

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ABSTRACT: Coexisting carotid artery stenosis and coronary artery disease is common and there is currently no consensus in treatment guidelines on the timing, sequence and methods of revascularization. We report a case of a patient with symptomatic triple vessel coronary artery disease as well as asymptomatic severe right internal carotid artery stenosis. Our patient underwent myocardial revascularization first, because she presented with unstable angina and was asymptomatic neurologically. This article summarizes current literature about the approach to carotid and coronary artery revascularization and addresses the decision-making process regarding the timing and sequence of revascularization.

KEYWORDS: Carotid artery stenosis, coronary artery disease, carotid endarterectomy, carotid artery stenting, coronary artery bypass graft, percutaneous coronary intervention

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Introduction

Coexisting carotid artery stenosis and coronary artery disease (CAD) is frequent, with prevalence of significant carotid lesions in patients undergoing coronary artery bypass graft (CABG) reported as high as 8% to 14%.[1] In patients undergoing carotid endarterectomy (CEA), the prevalence of CAD is 40% to 50%.[2] There is a risk of stroke in patients undergoing CABG (1.4%-3.8%)[3] and a risk of myocardial infarction in patients undergoing CEA (0%-2%).[4]

There is currently no consensus in treatment guidelines on the sequence of revascularization. Treatment strategies include (1) *Combined* or synchronous surgery, where CABG and CEA are performed in the same procedure or anesthetic setting; (2) *Staged* surgeries, consisting of CABG with subsequent CEA or CEA with subsequent CABG; (3) *Hybrid* procedures, which can be synchronous or staged, and consist of CABG with carotid artery stenting (CAS) or PCI with CEA and (4) *Transcatheter* procedures combining PCI with carotid artery stenting.

The etiology of stroke which occurs with CABG is multifactorial and includes the following: hypoperfusion due to hypotension in the presence of a severely stenotic carotid artery, micro-embolization from an ulcerated carotid plaque, as well as macro-embolization from ascending aorta atherosclerosis. In addition, many risk factors for stroke co-exist in CABG patients.[5]

Case report

A 55-year-old woman with insulin-dependent diabetes mellitus, hypertension, hyperlipidemia, peripheral vascular disease and severe triple vessel CAD status post 3-vessel stenting presented with anterior NSTEMI. Her EKG showed new T-wave inversions in V1-V4. A transthoracic echocardiogram demonstrated normal ejection fraction. There were no neurologic symptoms.

Coronary angiography demonstrated triple vessel disease, with severe LAD stenosis (shown in Figure 1) as well as high grade LCX and RCA lesions. In preparation for surgery, screening carotid doppler sonography showed severe stenosis of the right internal carotid artery (RICA). Carotid angiography showed 90% stenosis of the RICA (shown in Figure 2) and 50% stenosis of the left internal carotid artery (LICA).

It was decided to proceed with single CABG utilizing LIMA to the LAD and to defer stenting of the other coronary lesions. The plan was to treat the carotid disease after myocardial revascularization and resolution of active myocardial ischemia. Ten days after CABG, the patient again presented with recurrent severe unstable angina and repeat coronary angiogram showed a kink and insertion site stenosis in the LIMA which had been inserted proximal to the LAD lesion (shown in Figure 3). PCI of the LIMA/LAD was performed with excellent results and complete relief of symptoms (shown in Figure 4).

Attention was then shifted to the carotid lesion, and a stent was placed in the RICA with excellent angiographic results (shown in Figure 5). She experienced hypotension for approximately 12 hours as a result of baroreceptor response requiring low dose vasopressors. There was no myocardial ischemia during this period.

Methods

Literature review was accomplished by searching MEDLINE using Pubmed, Cochrane, and Dynamed. Searches included the words "carotid artery disease," "coronary artery disease," "carotid and coronary artery disease," "carotid artery stenting," "carotid endarterectomy," "percutaneous coronary intervention"

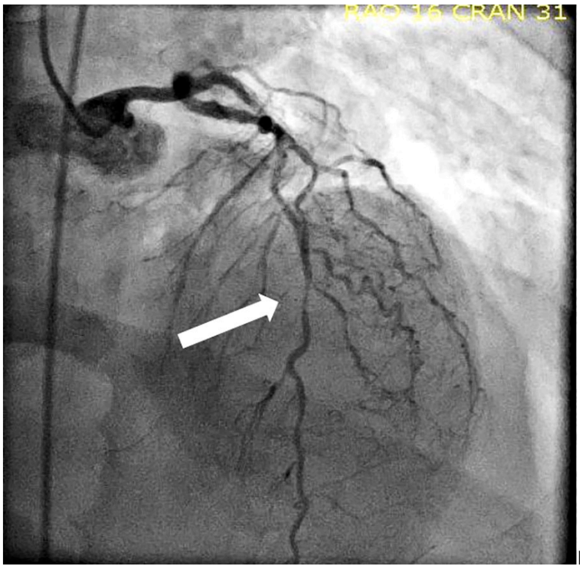

Figure 1. Coronary angiography during unstable angina demonstrated triple vessel disease with multiple prior stents and LAD with diffuse disease and severe stenosis (arrow) which was thought to be the culprit lesion.

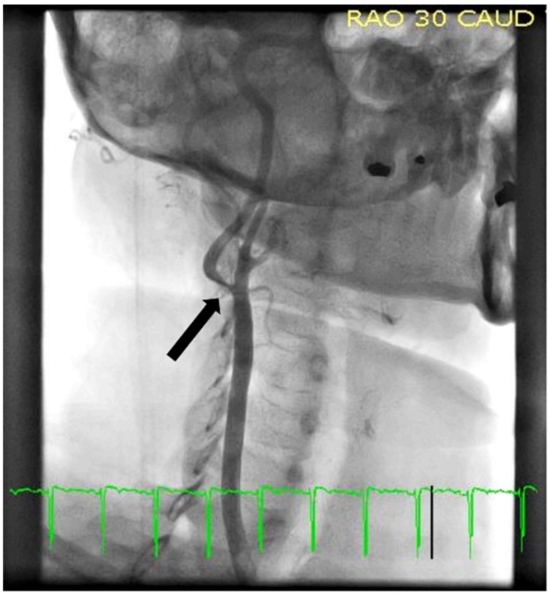

Figure 2. Carotid angiography prior to CABG showing the right internal carotid artery with severe stenosis at the ostium (arrow).

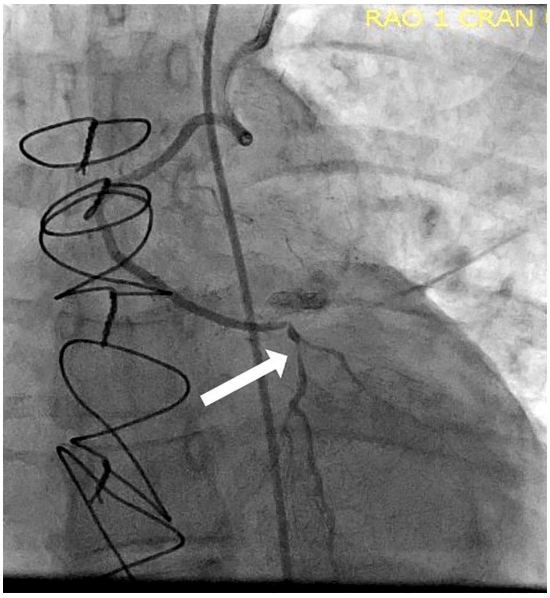

Figure 3. Coronary angiography after LIMA-LAD coronary artery bypass surgery. There is a severe kink in the LIMA anastomosis which was inserted proximal to the LAD lesion (arrow). This resulted in recurrent severe unstable angina.

Figure 4. Coronary angiography after LIMA-LAD coronary artery bypass surgery. This shows the result after percutaneous coronary intervention of LIMA-LAD. A drug eluting stent spans the kink and the lesion.

and "coronary artery bypass graft" and combinations of the above. Literature was reviewed and selected based on several factors such as number of patients involved, journal published, and ability to answer clinical question.

Screening for carotid artery stenosis in patients undergoing CABG

Who should be screened?

The ACC/AHA Guidelines for CABG (2011)[6] state that carotid artery duplex scanning is reasonable in selected patients who are considered to have high risk features (e.g., age >65 years, presence of a carotid bruit, left main coronary artery stenosis, peripheral artery disease, hypertension, smoking, diabetes mellitus, history of cerebrovascular disease (transient ischemic attack, stroke), history of cervical carotid disease) (Class IIa, Level of Evidence: C). These recommendations are based on a few observational studies.

Options for screening for carotid artery disease

The initial screening test is carotid duplex sonography which is widely available and has excellent sensitivity (94%) and specificity (92%) to detect carotid artery stenosis at 60% to 99%.[7]

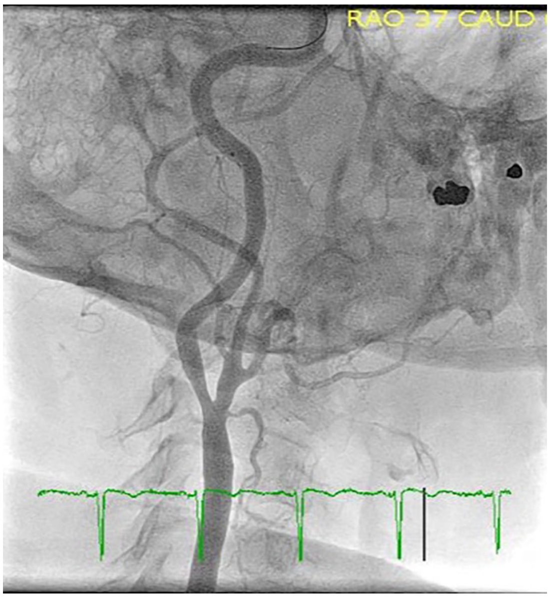

Figure 5. Treatment of internal carotid stenosis after resolution of angina symptoms with self-expanding stent placement with cerebral protection device.

When duplex sonography cannot be obtained, is equivocal or when additional anatomical information is needed, for example, for when an intervention is planned, CT-Angiography (CTA) or MR-Angiography (MRA) are other non-invasive diagnostic test options. Grading of the stenosis is most often based on the North American Symptomatic Carotid Endarterectomy Trial (NASCET) criteria. However, MRA often overestimates the degree of stenosis and assessment of calcified lesions with CTA is limited. Both CTA and MRA present difficulties in distinguishing subtotal and complete arterial occlusion.[8]

When non-invasive tests are inconclusive and additional anatomic detail is needed, catheter-based contrast angiography can be considered. In practice, duplex sonography and CTA or MRA are most often sufficient for adequate estimation of stenosis, and catheter-based angiography is used with the option of therapeutic intervention in the form of carotid artery stenting.[9]

Is there a benefit in screening?

Multiple clinical trials comparing CEA with medical therapy in patients with atherosclerotic stenosis of extracranial carotid arteries have favored carotid revascularization (namely NASCET[10] and ECST[11] in symptomatic carotid disease and ACST[12] and ACAS[13] in asymptomatic carotid disease).

A systematic review by Naylor et al[14] found an association between the degree of carotid stenosis and stroke risk in CABG patients, ranging from >2% in patients with no significant carotid disease up to 11% in patients with carotid occlusion (see Table 1). Interestingly, in Naylor's review,[14] 50% of stroke sufferers did not have significant carotid disease and in 60% the anatomic territory on CT scan or autopsy did not correspond to the region supplied by the affected carotid stenosis.

Table 1. Association between degree of carotid stenosis and stroke risk in patients undergoing CABG. According to Naylor et al.[14]

DEGREE OF CAROTID STENOSIS	PERI-CABG STROKE RISK
No significant carotid disease	<2%
>50%-99% unilateral stenosis	3%
>50%-99% bilateral stenosis	5%
Carotid occlusion	7%-11%

Who should undergo carotid revascularization?

Several factors have been shown to favor combined carotid and coronary revascularization, including (but not limited to) severe carotid artery disease, unfavorable morphological characteristics of the carotid lesion (eg, ulceration), presence of related symptoms and a history of TIA or stroke.[6] Patients with a history of TIA or stroke and severe carotid artery stenosis have a higher risk of post-CABG stroke and will likely benefit from revascularization.[15] The ACC guidelines comment that timing and sequence of carotid and coronary revascularization is based on the absence or presence of clinical symptoms.[6]

On the other hand, CABG alone can be performed safely in patients with asymptomatic unilateral carotid stenosis as revascularization offers no significant reduction in risk of stroke or death in these individuals.[6]

Carotid endarterectomy versus carotid artery stenting

CEA remains the standard of care for most patients with severe extracranial carotid disease. There are multiple clinical trials comparing carotid artery stenting and carotid endarterectomy with short-term and long-term follow up results, for example, the SAPPHIRE trial from 2004,[16] the European trials EVA-3S in 2008 and 2014[17,18] and SPACE in 2006 and 2009,[19,20] and most recently the CREST trial in 2010 and 2016.[21,22]

A systematic review of short term results of these trials showed an increased risk of stroke with CAS compared to CEA (RR 1.45; 95% CI 1.06-1.99; I^2 = 40%) but a decreased risk of periprocedural MI (RR, 0.43; 95% CI, 0.26-0.71; I^2 = 0%).[23]

Despite the higher risk of periprocedural stroke, carotid artery stenting has been accepted as a viable alternative to carotid endarterectomy in high risk patients and has gained popularity in recent years after CREST publication. A study by Otite et al. showed an increase of the utilization of CAS in patients older than 70 years from 11.9% in the pre-CREST to 13.8% in the post-CREST era (P = .005).[24]

However, there are no randomized controlled trials comparing CAS and CEA in patients who require coronary revascularization.

Tables 2–4 show high risk features for CEA and CAS as well as advantages and disadvantages of CAS compared to CEA.

Table 2. Clinical and anatomic features that determine a high risk for complications from carotid endarterectomy (CEA).[25]

HIGH RISK FEATURES FOR CEA	
ANATOMIC	COMORBIDITIES
Previous CEA with recurrent stenosis	Congestive heart failure (class III/IV) and/or known LVEF <30%
Contralateral carotid occlusion	Open heart surgery needed within 6 weeks
Contralateral laryngeal nerve palsy	Recent myocardial infarction (>24 h and <4 weeks)
Radiation therapy to neck	Unstable angina
High cervical ICA lesions or CCA lesions below the clavicle	Severe pulmonary disease
Severe tandem lesions	Age >80 years

ICA, internal carotid artery; CCA, common carotid artery; LVEF, left ventricular ejection fraction.

Table 3. Plaque and anatomic features that determine a high risk for complications from carotid artery stenting (CAS). Adapted from Noiphithak et al.[26]

HIGH RISK FEATURES FOR CAS	
PLAQUE MORPHOLOGY	VESSEL ANATOMY
Soft, lipid-rich plaque	Aortoiliac tortuosity
Extensive plaque (>15 mm)	Arch type II or III anatomy
Intraplaque hemorrhage	Bovine configuration
Thin fibrous cap	Arch disease
Heavy calcified plaque	Proximal or distal ICA tortuosity
Preocclusive lesion	
Stenosis at the bifurcation involving both the ICA and ECA	
Lesions located at the curve	

ICA, internal carotid artery; ECA, external carotid artery.

Table 4. Advantages and disadvantages of carotid artery stenting (CAS) compared to carotid endarterectomy (CEA).

ADVANTAGES AND DISADVANTAGES OF CAS	
ADVANTAGES	DISADVANTAGES
Less invasive	Risk of kidney injury
No risk for potential cranial nerve injury	Not suitable for patients who cannot tolerate DAPT
No arterial incision needed	Higher risk of stroke
Shorter hospital stays	
Lower risk of myocardial infarction	

DAPT, dual antiplatelet therapy.

Treatment strategies for combined carotid and coronary artery disease

CEA and CABG

Carotid endarterectomy and CABG can be performed simultaneously or in a staged approach (CEA then CABG, CABG then CEA). In general, simultaneous or synchronous procedures are reserved for patients with both acute coronary syndrome and cerebrovascular symptoms.[6]

There are no randomized controlled trials that determine whether a simultaneous or staged approach is favorable, but there have been multiple systematic reviews and meta-analyses over the years with comparable outcomes. Most recently, Tzoumas et al[27] ascertained a significantly higher risk for stroke (OR 1.51, 95% CI 1.34-1.71, $I^2 = 0\%$) and death (OR 1.33, 95% CI 1.01-1.75, $I^2 = 47.8\%$) but a lower risk of MI (OR 0.15, 95% CI 0.04-0.61, $I^2 = 0\%$) with the simultaneous compared to staged approach.

An earlier review[28] showed similar results, which suggested that simultaneous procedures had an overall higher risk for death and any stroke (8.7%, 95% CI 7.7-9.8) compared to staged CEA and CABG (6.1%, 95% CI 2.4-9.2), but none of the comparisons reached statistical significance. However, when the risk of periprocedural MI was subsequently included in the analysis, the risk of overall complications was higher with the simultaneous approach compared to the staged approach (simultaneous = 11.5% [95% CI 10.1-12.9], staged CEA + CABG = 10.2% [95% CI 7.4-13.1]).

This meta-analysis also analyzed outcomes for reverse staged CABG + CEA, meaning performing CABG first and then CEA, and found that there is a higher risk of stroke compared to simultaneous CABG + CEA or staged CEA then CABG.

CAS and CABG

Combining carotid artery stenting and CABG has gained popularity. These procedures can also be done simultaneously or staged. When done simultaneously, the operating room needs to be equipped with an angiography system and an experienced proceduralist should perform the procedure.

When CAS is performed prior to CABG, there is need for initiation of dual antiplatelet therapy (DAPT), which should be continued for a minimum of 30 days (preferably 3 months) after CAS.[8] In that case, CABG needs to be deferred for 4 to 5 weeks, which is problematic in patients with active myocardial ischemia.

No randomized controlled trials have compared simultaneous CAS + CABG to staged CAS then CABG. A review and meta-analysis by Paraskevas et al.[29] of 2727 patients, of whom 80% were neurologically asymptomatic, has shown similar mortality of staged CAS + CABG (4.8%, CI [3.3–6.8]) and simultaneous (meaning same-day) CAS + CABG (4.5%

[2.9–7.0]). Besides, there was a higher risk of stroke (5.4% vs 3.4%) and MI (4.2% vs 1.8%) with staged CAS + CABG compared to same-day procedures.

The higher risk of MI in staged CAS and CABG can be atttributed to reflex hypotension and bradycardia after CAS, which may worsen myocardial perfusion. Therefore, in patients which myocardial ischemia, CABG may be performed prior to CAS or same-day procedures can be considered.

The authors noted that the study groups were largely heterogenous regarding the risk profile of patients, the length of dual antiplatelet therapy (DAPT), the use of cerebral protection devices and the use of off-pump bypass.

Comparison of CEA and CAS in CABG

A serial, cross-sectional study conducted by Feldman et al[30] examined 22 501 patients from the Nationwide Inpatient Sample database from 2004 to 2012 who had any of the following three revascularization methods during the same hospital admission: (1) combined CEA + CABG; (2) staged CEA + CABG; and (3) staged CAS + CABG. The primary composite endpoints were in-hospital all-cause death, stroke, and death or stroke.

The authors found significantly lower rates of in-hospital death in CAS + CABG (1.9% vs 4.4% in combined CEA + CABG and 3.8% in staged CEA + CABG, $P < .01$), but no statistically significant difference for stroke rates between all three groups.

They also determined that CAS was generally performed in a higher risk cohort: in older patients, in patients with symptomatic carotid disease and in patients with a higher number of cardiovascular comorbidities such as hypertension, diabetes and chronic renal failure.

To better analyze the outcomes over time the authors divided the study group into two time periods (2004-2008 and 2009-2012). The greatest improvement in outcomes over time was seen in the CAS + CABG group, the unadjusted rates of death (3.5% vs 1.0%; $P = .02$), stroke (5.2% vs 1.7%; $P < .01$) and death or stroke (7.0% vs 2.7%; $P < .01$) were significantly lower in later years (2009-2012) than in earlier years (2004-2008).

The improved outcomes in CAS + CABG over time can likely be explained by the more widespread use of embolic protection devices and more experienced interventionalists.

In addition, the overall number of procedures for CEA was decreasing over the time of the investigation, while the procedural rates for CAS remained fairly stable.[30]

CEA and PCI

As previously mentioned, there is a high risk of MI in patients undergoing CEA before CABG (10.2% in patients undergoing CEA then CABG according to Tzoumas et al[27]).

In a trial conducted by Illuminati et al,[31] 426 patients without history or symptoms of CAD as well as normal EKG and echocardiogram, were randomized to undergo coronary angiography before CEA. There was a significantly reduced risk of MI in those with coronary angiography and intervention after the mean follow up of 3.5 years (HR.078; 95% CI, 0.024-0.256; $P < .001$) as well as a higher survival in the intervention group (95.6 ± 3.2% in the intervention group vs. 89.7 ± 3.7% in the non-intervention group, log-rank = 6.35, $P = .01$). Mortality specifically related to MI was also significantly lower in the intervention group (n = 0/216) compared to the non-intervention group (n = 6/210, $P = .01$).

The authors concluded that in patients with asymptomatic coronary artery disease, systematic coronary angiography followed by selective PCI or CABG prior to CEA significantly reduces the incidence of late MI and increases long-term survival.

However, the need for DAPT after PCI delays carotid intervention with CEA.

CAS and PCI

The risk of periprocedural stroke during PCI is low at 0.3% to 0.38%, but associated with increased mortality.[32,33] There is no data that suggest an increased risk of stroke in patients with concurrent carotid and coronary artery disease undergoing PCI. Hence, screening for carotid artery disease in patients undergoing PCI is not recommended.

A prospective, multicenter, non-randomized study conducted in 239 patients with concomitant carotid and coronary artery disease treated with staged or simultaneous carotid artery stenting and percutaneous coronary intervention showed outcomes similar to hybrid or surgical procedures. The reported rate of death, myocardial infarction, and stroke at long-term follow-up (median 520 days) was 4.2%, 2.1%, and 3.8%, respectively.[34]

This goes along with other studies[35,36] which concluded that simultaneous and staged CAS and PCI can be performed safely in patients with known carotid and coronary artery disease, with the timing and sequence of the procedures determined by the patient's anatomy and symptoms. The combination of PCI and CAS is particularly important in patients with high surgical risk.[36]

In contrast to hybrid procedures,[37] in patients with recent angiographic intervention requiring dual antiplatelet therapy, both PCI and CAS can be performed safely without interruption of the DAPT.[34]

Our case demonstrates a successful approach with CAS after PCI.

Conclusion

Coexisting carotid and coronary artery disease is common, and the timing and sequence of myocardial and carotid revascularization is controversial.

While many meta-analyses and reviews compare the rates of death, stroke and MI in different approaches, attention should be shifted to the individual patient: *Which vascular bed is symptomatic? Which approach does the anatomy allow? What are the individual risk factors?*

Our patient underwent myocardial revascularization before carotid stenting because she presented with unstable angina and was asymptomatic neurologically. This approach is consistent with recent guidelines, which suggest treating the more symptomatic region first.[6] Advances in technology allow a minimally invasive approach in selected patients with appropriate anatomy.

Recently, there is discussion whether screening for carotid disease in patients scheduled for CABG is beneficial.[38,39] About 90% of carotid revascularizations are done in neurologically asymptomatic patients and the risk of stroke in neurologically asymptomatic patients with a unilateral 70% to 99% stenosis undergoing an isolated CABG is extremely low. In addition, combining carotid and coronary revascularization overall increases morbidity and mortality, with a composite risk of death, stroke, or myocardial infarction within 30 days of combined CABG and carotid revascularization of 9% to 11% according to a review by Naylor.[39] The development of hypotension following carotid artery stenting may result in worsening myocardial ischemia in patients with active coronary lesions.

The literature used in this review consists of meta-analyses and reviews of retrospective studies or small case studies. There are several limitations, including very heterogenous study populations, whether patients were symptomatic or not, the timing of staged procedures ranging from days to several months and the use of DAPT. Furthermore, it is unclear in most of the retrospective trials what the exact morphology of the lesions were.

Randomized controlled trials are needed to further identify the ideal revascularization strategy in different patient groups. Our case demonstrates successful approach by re-vascularizing the more symptomatic vascular bed first.

Authors' Note

Part of the manuscript submitted has previously been presented at the 15th Annual Complex Cardiovascular Catheter Therapeutics (C3): Advanced Endovascular and Coronary Intervention Global Summit in June 2019 as a Poster (Case Report).

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I hereby confirm that I contain the rights to my work.

Author Contributions

All authors had access to data and were involved in writing the manuscript.

Compliance with ethics guidelines

This article is based on previously conducted studies and does not contain any studies with human participants or animals performed by any of the authors.

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