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Clopidogrel resistance in dual antiplatelet therapy after carotid stenting

We read with great interest the article by Ghamraoui et al[1] reporting about their favorable experience with the use of ticagrelor as part of dual antiplatelet therapy (DAPT) in 67 patients undergoing transcarotid artery revascularization (TCAR).

DAPT is the key treatment for patients undergoing carotid stenting, and current therapeutic regimens include a combination of acetyl-salicylic acid and a thienopyridine, the most used of which is clopidogrel.[2] However, the pharmacologic "resistance" to the effect of thienopyridines, which can affect about 30% of patients taking that drugs,[3] may increase the risk of periprocedural neurologic events and stent thrombosis.

The effect of alternative therapies have been studied mostly on patients with acute coronary syndrome undergoing coronary stenting, for whom ticagrelor has shown greater antiplatelet efficacy compared with clopidogrel.[4]

There are currently few studies on patients undergoing carotid stenting, for which the presence of an optimal DAPT aggregation is equally fundamental.

In their retrospective experience, Ghamraoui et al[1] did not observe major bleeding events or cerebrovascular ischemic events or death at 30 days postoperatively with the use of ticagrelor after TCAR. Therefore, the authors concluded that ticagrelor may represent a safe and effective alternative to overcome clopidogrel nonresponsiveness in DAPT regimens for TCAR.

Nevertheless, a control group of patients undergoing conventional DAPT regimen with clopidogrel is lacking. Ticagrelor has a well-known low rate of on-treatment platelet reactivity,[5] but its routine use in patients in whom clopidogrel may be properly effective may raise some cost issues. We agree with the authors about the need for a tailored approach in patients who should undergo DAPT after carotid stenting, but in our opinion this goal could be accomplished by performing platelet reactivity testing as part of routine care, and switching to ticagrelor in the event of thienopyridine resistance.

In our opinion, further studies are needed in the overall population of patients undergoing carotid stenting, to bring evidence either in favor or against the use of ticagrelor as an alternative therapy in clopidogrel nonresponsiveness.

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https://doi.org/10.1016/j.jvs.2021.04.076

Increased rates of ruptured abdominal aortic aneurysm during the COVID-19 pandemic

A significant reduction in arterial case volume entry has been reported by Natarajan et al in their recent article.[1] Screening for abdominal aortic aneurysm (AAA) in the general population and follow-up of patients with small AAA have been postponed.[2] The downstream consequences of delaying and reducing vascular visits and procedures remain undetermined. We have analyzed the reasons for the increased number of operations for ruptured AAA during the pandemic period (March 2020-April 2021) in our hospital, which is the only tertiary referral center in the province of Pavia (Lombardy) with 545,000 inhabitants. In the last 5 years, the population has been stable for number and mean age. Data of patients who had surgery for ruptured AAA during the pandemic period were prospectively collected and compared with those of patients who had surgery in the same period of the previous year. Elective and emergency arterial operations were reduced during the pandemic period (overall arterial operations, excluding accesses for dialysis, from 1000 to 630; emergency arterial operations from 200 to 160). The number of operations for ruptured AAA increased either for number or for percentage of emergency operations (12/200; 6% to 18/160; 11.2%). In the pandemic period, screening for AAA in the general population was not performed. Almost no patient without symptoms or with mild symptoms was referred for abdominal ultrasound or

computed tomography scan in the province of Pavia; follow-up visits for patients with small AAA were postponed in asymptomatic patients. Four patients suffered from AAA rupture during COVID-19 infection; 14 patients were negative for COVID-19 infection.

Two patients with the aneurysm maximum diameters of 65 and 68 mm were scheduled for surgery 40 and 45 days before rupture, respectively. Surgery was delayed for several reasons including the fear of the patient to get infected in an overwhelming outbreak pandemic period.

Another 6 patients with small AAA were followed with serial abdominal ultrasound studies that were postponed in the pandemic period. The remaining 10 patients did not know they had an AAA and they had no symptoms before the rupture.

A significant increase in mortality rates in the region Lombardy was documented for older people. Fifty percent of the increase was related to COVID-19 infection. The remaining 50% was not related to COVID-19 infection, and most deaths were caused by cardiovascular events. Despite the limits of a retrospective analysis and incomplete data about causes of mortality in the general population, our analysis supports the hypothesis of an increased incidence of ruptured AAA during the pandemic. The increased number of ruptured AAA is related to several risk factors: COVID19 infection triggers activation of metalloproteinases and digestion of the collagen of the aneurismal wall[3]; reduced number of abdominal ultrasound and computed tomography studies in the general population; postponed follow-up in patients with small AAA; patient reluctance to seek medical attention or delayed surgery because of patient fear or organizational problems.[4,5] We should add the stress and consequent arterial hypertension crises during the pandemic.[6]

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https://doi.org/10.1016/j.jvs.2021.07.224

The impact of alcohol on the levels of sex hormones and risk of developing abdominal aortic aneurysm

We found the article "Sex hormones in men with abdominal aortic aneurysm" by Villard et al[1] to be of great interest. This report examined the association between levels of sex hormones, such as total testosterone, estradiol, progesterone, luteinizing hormone, and sex hormone binding globulin, with the occurrence of abdominal aortic aneurysm (AAA) in elderly men.[1] Within this study, multiple variables were accounted for, such as smoking status, history of coronary heart disease, hypertension, diabetes, and kidney failure.[1] The report concluded that they were able to "identify a previously unknown association between progesterone levels and occurrence of AAA, even after consideration of other risk factors."[1] Although we acknowledge that these may be potential risk factors, there should be further investigation into alcohol as a factor influencing both the development of AAA and levels of sex hormones in elderly males.

Numerous studies have demonstrated that both acute and chronic alcohol use impacts the levels of sex hormones in animals and humans.[2] These studies have shown an increase in leutinizing hormone and estradiol levels with chronic alcohol use, whereas testosterone and progesterone are significantly decreased.[2] Furthermore, a meta-analysis on the relationship between alcohol and AAA has shown that alcohol can be both a potential risk factor and a protective factor for the development of AAA.[3] The relationship between alcohol and AAA appears to be a "tick-shaped trend" where below 2 units of alcohol consumption per day may be protective and above 2 units increases the risk of AAA.[3]

As alcohol is associated with both the levels of sex hormones in elderly men and the development of AAA, this creates a potential confounding variable within the study conducted by Villard et al.[1] We propose that a questionnaire that includes alcohol consumption as a factor be utilized, as this will enable the investigation into the impact of alcohol and address this potential confounding variable.

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