clinical outcomes (hazard ratio [HR] 2.01; 95% confidence interval [CI] 1.26 to 3.04; p = 0.004), whereas TTE (HR 1.11; 95% CI 0.78 to 1.55; p = 0.54), ARI <25 (HR 1.03; 95% CI 0.76 to 1.37; p = 0.87), and CT-ADP >180sec (HR 1.16; 95% CI 0.83 to 1.58; p = 0.38) were not associated with MACCE at 1 year (Figure 1). By multivariate Cox regression analysis, moderate-to-severe PVL by angiography was an independent predictor of 1-year MACCE (HR 1.96; 95% CI 1.22 to 3.00; p = 0.007).

Current trends of performing TAVR under local anesthesia make transesophageal echocardiography less suitable for PVL assessment. Although cine-angiography has been considered to be highly subjective, dependent on various technical factors and the observer's experience inducing variability in grading, TTE has been the most commonly used method to quantify PVL post-TAVR. However, this technology still has a number of shortcomings, partially due to the multiple, irregular, and eccentric paravalvular jets and the limited window according to patient positioning and interventional procedural factors. Misclassification of PVL grading by TTE was shown in a multicenter study with cardiac magnetic resonance, which demonstrated that PVL severity by cardiac magnetic resonance, but not by TTE, was associated with increased mortality and poorer clinical outcomes.[3] Likewise, there is a significant overlap between ARI and aortic regurgitation grades, which can be influenced by diastolic dysfunction, atrial fibrillation, and heart rate. The ARI ratio was suggested to overcome these limits, but its relationship with adverse outcomes was also not evidenced in the present study. Recent clinical study has reported that the CT-ADP >180sec could be a novel modality to detect PVL and predict 1-year mortality.[4] However, we previously described that this value could be influenced by the presence of a low hemoglobin level, low platelet count, and appropriate platelet inhibition by P2Y12-inhibitors.[5] Such factors may decrease the accuracy of CT-ADP in predicting clinical events among real-world TAVR patients. Overall, PVL measured by angiography was evidenced as the most meaningful modality in the prediction of adverse clinical outcomes in the present study. The grading of PVL remains challenging and future multicenter studies are warranted to ensure our findings in the current TAVR era.

Disclosures

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Association of Internet Use With the Use of Addictive Substances in the United States

Nicotine and tobacco products are strongly associated with cardiovascular diseases. Electronic cigarettes (e-cigarettes) have often been marketed as a safe alternative for smoking cessation,[1] which has led to their popular use over traditional combustible cigarettes. The past decade has also seen a ~20% increase in the use of Marijuana products.[2] We suspect that online marketing and social media advertisements may have a significant role to play in such trends.

We therefore conducted a cross-sectional study using data from the nationally administered Behavioral Risk Factor Surveillance System survey 2016 to 18 to identify the association between Internet use and pattern of substance use. Internet use was defined as use on 1 or more occasions in the past 30 days. Marijuana use was defined as use on 1 or more days in the past 30 days. Smokeless tobacco use was defined as use of chewing tobacco, snus, or snuff every day or on some days. Cigarette and e-cigarette use was defined as use on some days or every day. We used weighted multivariate logistic regression models to study the association of Internet use with the use of these substances.

Our study population consisted of 81% Internet users (n = 726,329) and 19% nonusers of Internet (n = 172,642). Compared to nonusers, Internet users were younger, more likely to be white, single, employed, and more educated. In multivariable analyses, Internet use

was positively associated [odds ratio (95% confidence interval, p value)] with current e-cigarette [2.40 (2.18 to 2.64, <0.001)], and marijuana use [1.77 (1.48 to 2.12, <0.001)], but inversely associated with smokeless tobacco [0.65 (0.60 to 0.70, <0.001)] and cigarette use [0.88 (0.84 to 0.91) <0.001)] .

In a contemporary and nationally representative U.S. cohort, we found that Internet users were more likely to use e-cigarettes and marijuana, and less likely to use cigarettes and smokeless tobacco. The widespread use of Internet and social media has likely resulted in newer avenues for advertisements and marketing,[3] with many states allowing online sales of e-cigarettes and marijuana products. The heterogeneity of state-specific legislature in regulating the online sale and use of these products, and the void created by the declining rates of traditional cigarette use could explain the rise in e-cigarettes and marijuana. Further, social media platforms like Instagram, Facebook, and Snapchat have many images of individuals, including celebrities, smoking marijuana, vaping etc. which may influence susceptible individuals such as young adults, to start using such products. These findings are important for health policymakers and healthcare providers alike as an avenue for primary prevention, and should be reported.

Disclosures

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Comparison of Oral P2Y12 Inhibitors in Acute Coronary Syndrome

Baldetti et al[1] have performed a network meta-analysis to compare oral P2Y12 inhibitors (clopidogrel, prasugrel, ticagrelor) in acute coronary syndrome. Seven randomized trials, along with some observational studies, were analyzed. The main efficacy end-point was a composite of major adverse cardiovascular events (MACE) at 12 months including cardiovascular death, myocardial infarction, and stroke (Table 5[1]). Other end points of efficacy (e.g., all-cause death at 1 year) were also evaluated. The odds ratio (OR) was the outcome measure. As regards 1-year all cause death, the results of this network meta-analysis favored prasugrel and ticagrelor compared with clopidogrel; prasugrel also reduced myocardial infarction rate compared with clopidogrel (Table 4[1]). The other end-points of efficacy (e.g., the MACE composite end-point) showed no significant differences among the 3 agents.

A wide literature has recently focused on some important disadvantages of both the hazard ratio and the OR (which are both relative outcome measures) particularly because, in pairwise comparisons, they tend to overemphasise the difference in favor of the more effective treatment.[2,3] Network meta-analyses are known to accentuate this tendency of OR.

In a separate report,[2] we have presented the narrative results that we obtained by analyzing the same 7 randomised trials assessed by Baldetti et al (15 patient cohorts; data from page 17 of the Supplementary Appendix[1]). Our rankings in effectiveness (based on event-free rates at 12 months; event = MACE) were estimated by simple arithmetic ordering. Since these results separately rely on the 15 patient cohorts, they lost their linkage with the inclusion criteria of the 7 trials and with the effects of randomisation.

The results in these 15 cohorts were the following: prasugrel ranked 1st, 4th, 6th, 9th and 13th; clopidogrel ranked 2nd, 7th, 8th, 14th and 15th; ticagrelor ranked 3rd, 5th, 10th, and 12th. The message arising from these results is that the effectiveness of clopidogrel, prasugrel, or ticagrelor has clearly a random distribution; hence, a network meta-analysis is unable to provide any meaningful information beyond the one provided by this narrative analysis. It should be noted that the assumptions of our reanalysis (e.g., transitivity of outcomes) are the same as those implicitly adopted by Baldetti et al[1] in their network meta-analysis.

As pointed out by Westafer and Schriger,[3] all network meta-analyses are based on the transitivity property and therefore assume that participants and trials are similar enough so that patients could have been randomized to any of the treatment arms. This allows the direct and indirect comparison to be made in any combination of between-treatment comparisons. Although meta-analyses are sometimes considered the ultimate form of evidence, the results are only as good as the underlying studies.[3] Ideally, any meta-analysis would include only those studies that are conducted on similar populations and use similar interventions; this is particularly important in network meta-analysis for the treatment effects to be transitive and determine reliable indirect estimates.

Coherence and/or network consistency is a unique component to evaluation of a network meta-analysis. So, network meta-analyses must be scrutinized for inconsistency, heterogeneity of trials or patient populations and potential sources of bias.

The overall picture emerging from our narrative analysis (in particular, our rankings) is a message of heterogeneous effectiveness across clopidogrel, prasugrel, or ticagrelor thus emphasising the potential inconsistencies of these 7 randomized trials. Although Baldetti et al presented a conclusion about comparative effectiveness favoring prasugrel, this conclusion is not supported by our results. In our view, our narrative analysis is simpler and more reliable than the unavoidably