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EDITORIAL

Is moderate drinking as effective as cholesterol lowering in reducing mortality in high-risk coronary patients?

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This editorial refers to 'Alcohol and long-term prognosis after a first acute myocardial infarction: the SHEEP study' by I. Janszky et al., on page 45

Most physicians know that alcohol drinking during pregnancy is criminal. Drinking before driving is just as criminal. We all know that chronic heavy drinking can result in liver cirrhosis or Wernicke–Korsakoff syndrome, and that even exceptional binge drinking can result in violence, unsafe sex, and cardiac death. On the other hand, the medical and scientific literature shows that moderate drinking (1–2 drinks/day for women and 2–4 drinks/day for men) is associated with a better life expectancy in the general population as well as in patients with established coronary heart disease (CHD).[1–3] The study by Janszky *et al.*[4] is an additional report showing the protective effect of moderate drinking in Swedish patients after acute myocardial infarction (AMI). In the absence of a controlled trial, which is neither technically nor ethically feasible, the main question for physicians remains whether the inverse association between moderate drinking and CHD complications is a cause–effect relationship. If it is, what should cardiologists do with their patients at risk of dying from AMI?

This editorial focuses on patients at high risk of dying from a recurrent heart attack. The authors do not intend to discuss the alcohol issue in the general population or the established fact that patients at very high risk need an implantable cardiac defibrillator (ICD).

Some scientists and physicians think that most studies reporting alcohol-induced protection are biased. The main bias is called 'sick quitter bias', meaning that non-drinkers (the referent group in most studies) include former drinkers who have recently stopped drinking due to illness.[4] That disease in former drinkers may explain the higher risk among the whole group of non-drinkers as compared with moderate drinkers. Although previous prospective studies with light drinkers (rather than non-drinkers) as the referent group have shown that the 'sick quitter bias' is not the main explanation for the protective effect of moderate drinking, this study by Janszky *et al.*, in which former drinkers were examined separately from long-term abstainers, actually confirms that protection is still present when only long-term abstainers are included in the referent group.[4]

This is an important finding because it strongly supports the cause–effect relationship between moderate alcohol drinking and better survival. However, there are technical limitations in that study, including small sample size (and a small number of former drinkers), a small number of (cardiac) deaths, and a quite short follow-up, but these converge to weaken the inverse association between moderate drinking and better survival, and hence further support a cause–effect relationship. It is therefore not unexpected that protection appears to be less significant in that small Swedish cohort than in other populations or in meta-analyses where moderate drinking generally results in ~30% less cardiac mortality and a 20% reduction of all-cause mortality,[1–3] which is considerable when compared with the effect of drug treatment (see below) and in terms of public health.

In addition to the strong epidemiological evidence (and in the absence of clinical trials), another way of evaluating the type of relationship between moderate drinking and survival is to examine the biological mechanisms by which moderate alcohol consumption may reduce the risk of cardiac death and improve

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survival. Beside the well-known effects of alcohol on high-density lipoprotein (HDL)-cholesterol, haemostasis (through reduced platelet function and fibrinogen levels), and insulin resistance, which are discussed by Janszky *et al.*, [4] recent data indicate that moderate drinking may have a direct protective effect on the ischaemic myocardium,[5] and may positively interact with ω-3 fatty acids[6] known to be highly protective in secondary prevention, especially against sudden cardiac death (SCD) and in populations with relative (or major) deficiency in ω-3 fatty acids.[7]

It is important to determine these two mechanisms because they may partly explain why moderate drinking was shown to reduce the risk of SCD,[8] a CHD complication which accounts for 65–75% of all cardiac deaths in the US population.[9]

Thus, epidemiological and biological studies strongly suggest that moderate drinking results in reduced mortality and better life expectancy in patients with established CHD. May we advise cardiologists to be very pragmatic and give up ideological postures when considering strategies to protect their high-risk patients from dying of a recurrent heart attack? What are the evidence-based interventions? Smoking abstention, regular physical exercise, a Mediterranean diet (of which wine drinking is one of the major characteristics) and some drug treatments are certainly effective in reducing mortality, with the additional option of an ICD for patients at very high risk. Regarding drug treatment, anti-platelet agents are obviously protective, while the rather modest effect of β-blockers remains to be confirmed in the era of modern interventional cardiology. To get an idea of the potential of moderate drinking to protect our patients' lives, we must compare it with the effects of intense cholesterol lowering, which has become the cornerstone of prevention for many physicians.

Let us take a look at the high-risk patients tested in recent randomized trials where patients were benefiting from most recent advances in interventional cardiology and associated drug treatment. If we specifically look at the overall mortality outcome (the only end-point that can be easily verified through national death registries) and thus control for potential bias due to tight connections between investigators and sponsors,[10] what do we see?

Whereas in the first statin trials in post-AMI patients (4S and LIPID), mortality was indeed reduced, this was not confirmed in more recent trials conducted in survivors of a recent AMI (TNT, MIRACL, IDEAL for instance) or in patients after a recent stroke (SPARCL trial), or in diabetic patients on haemodialysis (the diabetics with the highest risk of cardiac death, in the 4D trial), where the numbers of deaths in the very low cholesterol groups were not significantly different from those in the control groups, despite striking differences in low-density lipoprotein (LDL)-cholesterol between groups in each trial. When adding all the deaths occurring in these trials (thus excluding the 'too small sample size' explanation when analysing each trial separately), the total numbers of deaths are respectively 1664 and 1670, showing no effect of intense cholesterol lowering on mortality. We must also keep in mind that in different clinical contexts, such as in primary prevention and in women with CHD, cholesterol lowering also has no effect on mortality.[11]

Thus, cardiologists should be aware that moderate drinking appears to be more effective than intense cholesterol lowering to protect the lives of their high-risk and post-AMI patients.[1–4] This is not totally surprising because cholesterol, in contrast to alcohol drinking, is not a mediator of platelet function, coagulation, fibrinolysis, thrombosis, leukocyte function and inflammation, the main mechanisms and pathways by which acute coronary obstruction, myocardial ischaemia, and SCD occur. Also, unlike alcohol drinking,[5,8] cholesterol lowering does not have any protective effect on the ischaemic myocardium and no effect at all on the risk of malignant ventricular arrhythmia and SCD, the main causes of cardiac death.[8,9,11]

Finally, cardiologists should remember that moderate drinking is a social lubricant and a major characteristic of the European lifestyle, often associated with the feeling of 'joie de vivre', especially in Southern Europe. They should keep in mind that they must not only protect the lives, but also preserve the quality of life of their fragile high-risk patients.

To summarize, for their CHD patients cardiologists should: (i) identify those at very high risk of cardiac death, for whom there is a clear indication for an ICD; (ii) identify binge and heavy drinkers and explain to them a better way of drinking to protect their lives; (iii) identify non-drinkers (and respect their choice), but also those who abstain because they wrongly believe that even light drinking is bad for their health; and (iv) explain to all patients (with or without ICD) that moderate and responsible drinking, especially (but not only) in the form of wine, is an effective way to prevent both fatal and non-fatal complications of CHD,[12] even in Northern Europe and in old age.[1,4,12]

Conflict of interest: none declared.

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CLINICAL VIGNETTE

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Percutaneous closure of false aneurysms of the aorta in Wiskott–Aldrich syndrome

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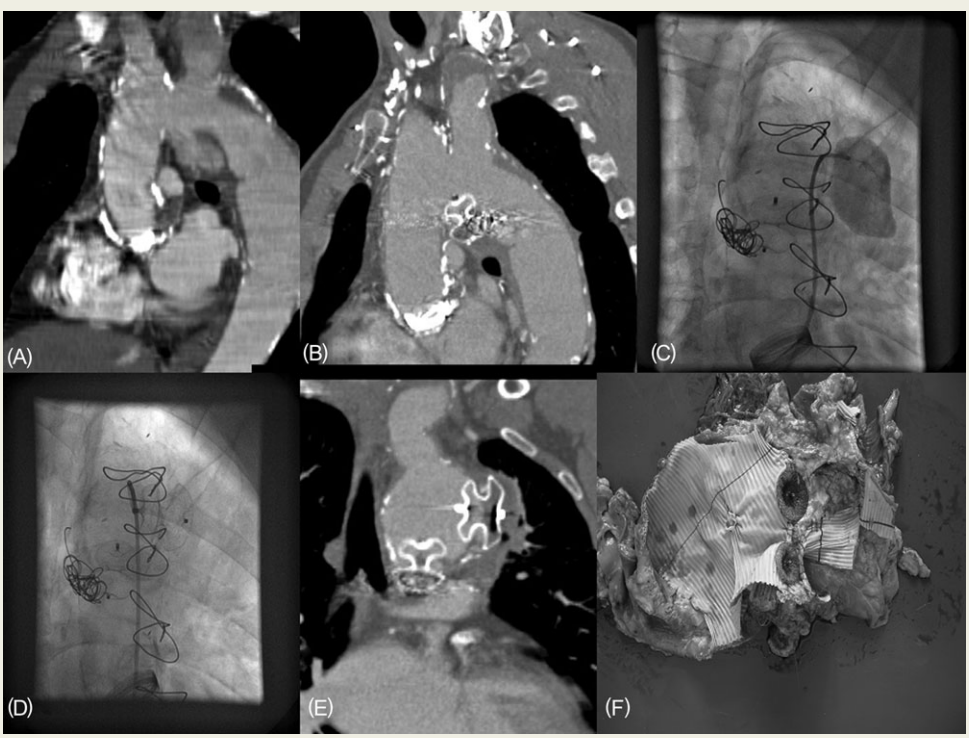

We report a 27-year-old man with Wiskott–Aldrich syndrome and aortitis causing severe aneurysmal dilatation. He underwent a two-stage composite graft replacement of aortic root and ascending aorta in 1998 and replacement of part of the distal aortic arch and descending aorta in 2003. Three years after the previous surgery, he was admitted with haemoptysis due to an aorto-bronchial fistula from a false aneurysm of the ascending aorta (Panel A).

Redo surgery was considered high risk, so he underwent percutaneous implantation of three IDC coils in the aneurysm and closure of the neck with a 13 mm Amplatzer septal occluder. CT scan at 4 weeks showed complete occlusion (Panel B).

Four months later, he had another haemoptysis and a second aneurysm in a different position had developed (Panel C).

The neck of the aneurysm was too large for coils, so an 18 mm Amplatzer septal occluder was implanted (Panel D).

Three weeks later, a routine CT scan showed appearance of air inside the 18 mm occluder, indicating patency of the fistula between the aneurysm and the bronchus (Panel E).

Twelve hours after CT, he had a catastrophic haemoptysis and died within an hour, without time for surgical or catheter intervention.

Autopsy revealed extension of the neck of the second aneurysm along the suture line. Both the Amplatzer devices were positioned correctly (Panel F).

The first aneurysm had organized thrombus in the cavity around the coils and no evidence of fresh bleeding.

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