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REVIEW

Publicizing the Cardiovascular Health Benefits of Donating Blood Could Help Alleviate the Blood Shortage

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ABSTRACT

A shortage in the supply of blood products developed in the United States following the coronavirus disease 2019 pandemic, but shortages have always affected some lower and middle-income countries. Donating blood reduces blood viscosity by lowering the hematocrit in the short term and promoting the replacement of older, stiffer erythrocytes with fresh, maximally deformable ones over the long term. It also reduces plasma viscosity. By lowering blood viscosity, blood donation protects against atherosclerotic cardiovascular disease and treats metabolic syndrome. Promoting the benefits of blood donation to the donor may help alleviate blood shortages.

Key words: Blood donation; Blood viscosity; Atherosclerotic cardiovascular disease; Metabolic syndrome

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INTRODUCTION

An adequate blood supply is essential for managing trauma, surgical, hematology, and oncology patients. A shortage of blood products leads to rationing and delays in elective surgery. Following a drop in blood donations attributed to the coronavirus disease 2019 pandemic, in January 2022 the American Red Cross declared a "blood crisis" for the first time. Even before the pandemic, a modeling study using data from the World Health Organization showed that 119 of 195 countries did not have an adequate blood supply. According to that model, shortages disproportionately affect low-income countries: every country in central, eastern, and western sub-Saharan Africa, Oceania, and South Asia, for example, had an inadequate blood supply[1].

LOWERING HEMATOCRIT AND BLOOD VISCOSITY REDUCES CARDIOVASCULAR RISK

A potential solution to the current blood shortage could be publicizing the possible health benefits of blood donation. Blood donation protects against atherosclerotic cardiovascular disease (ASCVD) because it lowers blood viscosity. In one study, hematocrit decreased from 44% to 41% (p-value not reported) and plasma viscosity decreased from 1.98 to 1.55 centistokes ($p < 0.05$) one week after donation[2]. Fresh erythrocytes are the most deformable, prolonging the decrease in blood viscosity from the pre-donation value[3].

In a meta-analysis of the effect of hematocrit on the risk of myocardial infarction (MI) and peripheral vascular disease, the

relative risk in the highest versus lowest tertile of hematocrit was 1.16 (95% confidence interval (CI) 1.05 to 1.29) in population-based studies and 1.81 (95% CI 1.19 to 2.76) in subjects with pre-existing ASCVD[4]. All studies were adjusted for age and sex, and most were adjusted for smoking and lipids. The effect of hematocrit on the risk of MI is considered to be one factor in decreasing the risk in premenopausal females. The risk of MI and peripheral vascular disease in the highest versus lowest tertile of plasma viscosity was 1.57 (95% CI 1.34 to 1.85) in population-based studies and 2.60 (95% CI 1.64 to 4.12) in subjects with pre-existing ASCVD[4].

Elevated blood viscosity was a strong risk factor for ASCVD in the Edinburgh Artery Study[5]. Blood viscosity was significantly higher in those who suffered a cardiovascular event, 3.70 centipoise versus 3.55 centipoise ($p = 0.0003$). This difference is much less than the viscosity reduction achievable by blood donation. A one standard deviation increase in blood viscosity raised the relative risk of an adverse event by 1.2 (95% CI 1.07-1.36). This was similar to the risk associated with elevated diastolic blood pressure and LDL-cholesterol and greater than that of cigarette smoking.

REVIEW OF PREVIOUS STUDIES OF BLOOD DONATION ON ASCVD

The therapeutic effect of an intervention varies with the prevalence of a disease. Family history, age, and gender are powerful risk factors for ASCVD. Family history is the most important independent risk factor for atherosclerosis. Atherosclerosis is usually silent until middle age or later, when the incidence of MI increases 5-fold between ages 40 and 60. Premenopausal women are relatively protected against atherosclerosis compared with age-matched men[6].

The strongest therapeutic effect of blood donation in preventing ASCVD was seen in the Kuopio (Finland) Ischaemic Heart Disease Risk Factor Study. Kuopio has a particularly high incidence of coronary artery disease (CAD). Almost half of the subjects had a family history of CAD, and subjects with CAD participated in the study. In this study, 2,862 men aged 42 to 60 were followed for an average of almost 9 years. One of 153 (0.7%) men who donated in the 24 months preceding the baseline examination experienced an MI, compared to 16 of 2,529 non-donors (12.5%) ($p < 0.0001$ for the difference between proportions). In a Cox proportional hazards model adjusting for age, examination years, and all other predictive CAD risk factors, blood donors had an 88% reduced risk of MI (relative hazard = 0.12, 95% CI 0.02-0.86, $p = 0.035$)[7].

In contrast, blood donation had no benefit in the Health Provider's Study [8]. Subjects were at low risk for ASCVD. Only 10 to 11 percent had a family history of MI. All subjects were male. The mean age of subjects was not reported. The study population was health-conscious: subjects expended an average of 35 to 37 metabolic equivalents exercising per week, and 18% to 21% took vitamin E supplements during the study period, 1992 to 1996.

In a study entitled "Cardiovascular risk in 159 934 frequent blood donors while addressing the healthy donor effect," frequent blood donation decreased ASCVD only in females[9]. Subjects were aged 29 to 36 at the start of participation, which was between the years 1990 and 1993, and followed between 90 to 118 months. The study population was at low risk for ASCVD because of age, normal blood pressure, and body mass index. One of the strongest risk factors in women of childbearing age is oral contraceptive use, which was associated with a 2-fold increased risk (95% CI 1.5-2.8) of MI in a study published in 2003[10]. Increased risk of MI because of oral contraceptive use in a subset of females could explain the benefit seen in high-frequency donors. Oral contraceptive use was not reported in the study. The healthy donor effect has been hypothesized by some to cause the benefit seen in some studies of blood donation. According to this notion, the benefit of blood donation is solely because successful donors have a decreased risk of ASCVD because of pre-donation screening. This study was designed to uncover such an effect and found no evidence of it.

These apparently discrepant results are really the expected outcomes when an effective intervention is used in both high- and low-prevalence populations. A large effect is noted in the former and a smaller effect in the latter. These results can be interpreted to show that blood donation is an effective intervention for ASCVD. A healthy donor effect is not necessary to account for the benefit seen in some studies.

THERAPEUTIC PHLEBOTOMY AND METABOLIC SYNDROME

People deferred from donating blood can undergo therapeutic phlebotomy, which differs from blood donation only in intent. In a prospective randomized trial of subjects with metabolic syndrome, two rounds of therapeutic phlebotomy decreased plasma glucose by 12.5 mg/dL compared to 2 mg/dL in controls. Blood pressure decreased by 18.3 mm Hg in subjects and only 0.2 mm Hg in controls. At entry, 300 mL of blood was removed, and between 250 and 500 mL were removed four weeks later[11]. Lower blood viscosity improves perfusion of skeletal muscle, increasing glucose uptake by myocytes and decreasing postprandial plasma glucose concentrations. Reducing blood viscosity decreases systemic vascular resistance and lowered blood pressure. In subjects with metabolic syndrome, these beneficial effects cannot be attributed to a putative healthy donor effect.

THE RISK-BENEFIT RATIO OF BLOOD DONATION FOR DONOR AND RECIPIENT IS VERY HIGH

Received wisdom holds that the safest blood products are from altruistic donors because incentives could motivate people to hide risk factors that might make their donation less safe. However, screening strategies and post-transfusion surveillance for blood-borne illnesses are so effective that the United States Food and Drug Administration (FDA) was able to shorten the deferral for men who have sex with men from 12 months of abstinence to 3 months. Given this capability, it is difficult to imagine how donations from people motivated to improve their health could be riskier than any other.

Only one possible donation-associated death was reported to the FDA in Fiscal Year 2015, the most recent data available. In 2019, there were 805,000 MI and 360,900 deaths due to CAD in the US. The benefit-to-risk ratio of blood donation as an intervention for ASCVD is potentially very high. There is no question that recipients of blood donation benefit and preliminary data evidence shows that donors benefit as well. The real question physicians should ask is, "Is it ethical *not* to promote the possible health benefits of donating blood?"

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