Cardiovascular risk stratification in young women: the pivotal role of pregnancy

Anna Vittoria Mattioli[a,*], Francesca Coppi[a,*], Valentina Bucciarelli[b,*] and Sabina Gallina[c,*]

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[a]Department of Medical and Surgical Sciences for Children and Adults, University of Modena and Reggio Emilia, Modena, [b]Cardiovascular Sciences Department-Azienda Ospedaliero-Universitaria delle Marche, Ancona and [c]Department of Neuroscience, Imaging and Clinical Sciences, 'G. d'Annunzio' University of Chieti-Pescara, Chieti, Italy

Correspondence to Prof. Anna Vittoria Mattioli, Department of Medical and Surgical Sciences for Children and Adult, University of Modena and Reggio Emilia, Via del pozzo, 71 41100 Modena, Italy
E-mail: annavittoria.mattioli@unimore.it

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Quantification of cardiovascular risk in women is a complex phenomenon. Two reasons can be identified: the effects of traditional cardiovascular risk factors change at different stages in women's lives, and female-specific risk factors have been identified and should be evaluated.[1] In recent years, knowledge of the risk that develops in the menopausal transition and menopause has been extensively studied; in contrast, the risk related to the early stages of life of young women and adult women is less explored. Recently, much attention has been paid to pregnancy.[2,3]

Cardiovascular disease (CVD) is a significant concern in pregnant women, affecting approximately 1–4% of pregnancies in the USA. CVD is the leading cause of pregnancy-related mortality in the USA, accounting for over 33% of maternal deaths related to or aggravated by pregnancy.[4–6]

Furthermore, non-Hispanic American Indian/Alaska Native women have the second highest pregnancy-related mortality ratio according to the Pregnancy Mortality Surveillance System data (2007–2016).[7]

This commentary analyzes the three different moments of cardiovascular risk assessment before, during, and after pregnancy (Fig. 1).

Before pregnancy

Although the pathophysiology of pregnancy-related complications is complex and likely multifactorial, emerging data suggest that these complications have, at least in part, prepregnancy origins, highlighting the importance of identifying and managing cardiovascular risk factors early in pregnancy.[3,6,7]

The prepregnancy period may be a critical period for interventions to identify and manage cardiovascular risk factors in birthing individuals and their offspring.[3,6,7] Interventions during this period have great potential for benefit, as they can target risk factors that may contribute to adverse pregnancy outcomes (APOs) and subsequent CVD.[8,9]

Lifestyle can be analyzed by evaluating the Life's Simple 7. Originally defined in 2010, the Life Simple 7, which integrates seven health factors (diet, physical activity, no smoking, BMI, blood pressure, lipids, and blood sugar), was reviewed in Life's Essential 8, which incorporates sleep health as an eighth factor.[3,10]

Health before conception is influenced by a wide range of lifestyle aspects, one of which is diet. Healthy diets help reduce the risk of diet-related noncommunicable diseases (NCDs).[11–13] Several studies have observed associations between prepregnancy lifestyle and maternal and infant health outcomes.[11–14] Recent evidence also suggests that women's nutritional status prior to pregnancy is associated with maternal and infant outcomes.[15–20]

Furthermore, maternal nutrition is associated with intergenerational effects on NCDs risk in adult offspring.[21] Foundational determinants have been included at the basis of the approach for correct cardiovascular health before pregnancy: resilience/stress, social determinants, and structural policies.

The impact of stress on cardiovascular health has been re-evaluated in the pandemic and postpandemic period especially in frail, elderly people and women.[21–23] These individuals have a fragility largely determined by the poor socio-economic conditions that lead to incorrect lifestyles and a lack of prevention.[17,19–22]

Similarly, an increasing role of depression on cardiovascular risk, especially in women and during the COVID-19 pandemic, has been advocated.[23,24]

* All authors equally contributed to the development of the manuscript.

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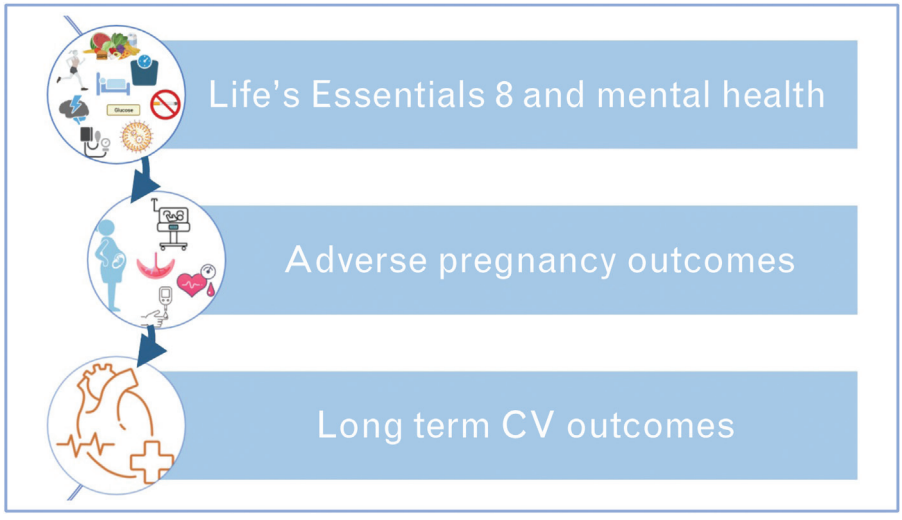
Fig. 1



The pathophysiological continuum of cardiovascular risk in young women. Before pregnancy, it is mandatory to identify CV risk factors and to pursue the CV health goals. Moreover, mental health should be monitored (top figure). Young women with CV risk factors and poor CV health are more prone to developing APOs which constitute additional risk factors for CVD and should be monitored closely after pregnancy (central and bottom figure).

Moreover, a significant association between prenatal depression and new CVD within 24 months postpartum has been described.[25]

During pregnancy

Pregnant women with CVD are at a higher risk of experiencing adverse cardiovascular outcomes, such as heart failure, arrhythmias, myocardial infarction, stroke, and aortic dissection.[3,6,26]

In addition, they are at an increased risk of obstetric complications, such as preterm delivery, gestational hypertension, and preeclampsia, which can further exacerbate their cardiovascular risk.[4–6] Therefore, it is crucial to identify and manage cardiovascular risk factors early in pregnancy and refer pregnant women with CVD to a multidisciplinary team of specialists for optimal management of their condition. This approach can help improve maternal and fetal outcomes and reduce the risk of long-term cardiovascular complications.[27]

Adverse pregnancy outcomes, which include hypertensive disorders of pregnancy (HDP), preterm birth, small-for-gestational-age (SGA) birth, and gestational diabetes, affect nearly one in five births currently. Rates of APOs have increased significantly over the past decade, with a near doubling in rates of HDP.[4–6]

Available data demonstrate a strong association between APOs and the risk of subsequent CVD, as detailed in the 2021 AHA scientific statement 'Adverse Pregnancy Outcomes and Cardiovascular Disease Risk: Unique Opportunities for Cardiovascular Disease Prevention in Women'. Emerging data also identify higher risk of long-term kidney disease among individuals who experience APOs, which is an important risk factor for CVD.[3]

Overall, recognizing and managing APOs is an important step in reducing the risk of CVD in women who have experienced these conditions during pregnancy.[28,29]

A recent study highlighted that the addition of Adverse Pregnancy Outcomes to the Framingham Risk Score improved the risk estimation of CVD.[27]

Furthermore, the risk or the presence of manifest perinatal depression should be accurately counseled. This condition affects as many as one in seven women during pregnancy or following childbirth and represents one of the most common issues of pregnancy and the postpartum period. Moreover, it can result in negative short-term and long-term effects on both the maternal and offspring's mental and physical health, probably related to an increase in pro-inflammatory cytokines and cortisol levels.[30] The USPSTF recommends that clinicians provide or refer pregnant and postpartum women who are at an increased risk of perinatal depression to counseling interventions, that is, physical activity.[31,32]

A different approach is proposed for women who already have CVD before pregnancy. This group of individuals is growing, thanks to the improvement of diagnostic methods and therapies.

Data from an analysis conducted on 39 212 104 pregnant patients in the time period 2010–2019 showed that 11.3% had CVD. That percentage had risen from 9.2% in 2010 to 14.8% in 2019. In-hospital all-cause mortality was 8.2/10 000 in the CVD group and 0.26/10 000 in the non-CVD group. Pregnant patients with CVD had 15.51 times higher odds of in-hospital all-cause mortality [95% confidence interval (95% CI) 13.22–18.20, $P < 0.001$] compared with those without CVD. Age-adjusted all-cause in-hospital mortality decreased among pregnant patients with CVD (from 8.1/10 000 in 2010 to 6.5/10 000 in 2019, $P < 0.001$) and without CVD (from 0.22/10 000 in 2010 to 0.21/10 000 in 2019, $P < 0.001$). Furthermore, CVD was associated with higher 6-week postpartum all-cause readmission, myocardial infarction, and stroke rates.[33]

The modified WHO (mWHO) classification of maternal cardiovascular risk is a classification schema that is widely used to help in counseling individuals with a preexisting cardiac disease considering or in pregnancy. This risk classification integrates all known maternal cardiovascular risk factors including underlying heart disease and comorbidity; however, preexisting IHD is not included in the current mWHO classification, despite evidence that the number of individuals with IHD who become pregnant is growing.[33,34]

After pregnancy

Women who experience APOs during pregnancy have an increased risk of developing CVD later in life.[28,35,36]

Women who developed APOs should be monitored closely and receive appropriate interventions to prevent or mitigate the development of CVD; specifically, they need to be more active and to adhere to a healthy lifestyle.[37] Early recognition, monitoring, and treatment of APOs are key to limiting CVD complications later in maternal life. For example, women with a history of gestational diabetes should be screened regularly for type 2 diabetes and other CVD risk factors.[38–40] Similarly, women with a history of hypertension during pregnancy should also be monitored closely and receive appropriate treatment to manage their blood pressure.[41–45]

Research has shown that women who experienced preeclampsia during pregnancy are at a higher risk of developing asymptomatic heart failure later in life. This increased risk persists even after accounting for traditional cardiovascular risk factors, such as high blood pressure, diabetes, and obesity.[46]

The exact mechanisms linking preeclampsia to heart failure risk are still being studied, but it is believed that the cardiovascular changes during pregnancy may have long-term effects on heart health.[47,48]

A common pathophysiological pathway has been identified linking preeclampsia and fetal growth retardation (FGR) to the development of heart failure with preserved ejection fraction (HFpEF) later in life. This pathway involves several interconnected mechanisms, including chronic inflammation, oxidative stress, vascular biological aging, and myocardial subclinical involvement.[49]

Preeclampsia and FGR are associated with an abnormal inflammatory response in the maternal body. Inflammation plays a crucial role in the development of endothelial dysfunction, which can impair blood vessel function and contribute to cardiovascular complications. Chronic inflammation can persist beyond pregnancy, leading to long-term vascular damage and promoting the development of HFpEF.[50]

During preeclampsia and FGR, there is an increased production of reactive oxygen species (ROS), leading to oxidative stress. Excessive ROS can cause damage to blood vessels and impair the function of the heart. Oxidative stress, if not properly balanced by antioxidants, can contribute to the progression of CVDs, including HFpEF.[50]

Preeclampsia and FGR are also associated with abnormalities in blood vessel structure and function. The vascular changes that occur during pregnancy may accelerate vascular biological aging, leading to stiffer and less elastic blood vessels. Vascular aging can contribute to increased vascular resistance and impaired diastolic function, which are characteristic features of HFpEF.[50]

Furthermore, during preeclampsia and FGR, the heart may be exposed to increased stress due to altered hemodynamics and increased systemic inflammation. This stress on the heart can lead to subtle structural and functional changes in the myocardium, even in the absence of apparent symptoms. Over time, these subclinical myocardial changes can progress and contribute to the development of HFpEF.[51,52]

These pathophysiological mechanisms provide insights into the potential long-term cardiovascular consequences of these pregnancy complications.

Pregnancy poses a challenge to the cardiovascular system with increased blood volume, pro-coagulation state and inflammatory factors, and insulin resistance.[53,54] This physiological stress is not complicated for most women, except for women who experience premature birth.[55]

This APO may serve to identify women at risk for CVD who would have gone undetected using traditional risk

assessment scores at a time when it might be possible to alter their risk trajectory.[56–58] It is unclear whether preterm delivery is an independent risk factor for future CVD or a marker of women at a high risk for future CVD. Because preterm birth is a heterogeneous condition with multiple causes, the pathogenesis of preterm birth remains poorly understood.[59] The main proposed mechanisms include increased systemic inflammation, infection, or vascular disease.[59]

In addition, interventions in the postpartum/interpregnancy period may offer a unique opportunity to address risk factors during the prepregnancy period before a subsequent pregnancy, potentially improving outcomes for both the mother and offspring. Overall, identifying and managing cardiovascular risk factors during these critical periods may be essential in reducing the burden of CVD in women.

Conflicts of interest

There are no conflicts of interest.

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