Abstract

Poor sleep patterns, including sleep restriction, are common, with 28% of the US adult population reporting 6 or fewer hours of sleep per night and those who do are 24% more likely to have cardiovascular disease. Women adopt such behavior in disproportionately greater numbers due to life-long demands on them as caregivers, first to their children and later to ailing and/or elderly family members. Retrospective data suggest an association between sleep restriction and increased cardiovascular events and prospective data show an increase in cardiovascular mortality. Thus, sleep deprivation may be a common and preventable cardiovascular risk factor in both pre- and post-menopausal women. Indirect evidence suggest that endothelial function is impaired in chronic sleep restriction. However, of the mechanisms underlying endothelial dysfunction, a key step in the initiation and progression of cardiovascular diseases, in sleep restriction remain unclear. In order to study endothelium directly, we have developed a minimally invasive technique of endothelial harvesting that allows direct examination of endothelial cells without the artifact of culture conditions in humans. We have a 12-year experience in conducting a direct endothelial assessment in healthy women and those with obesity, sleep apnea and heart failure. Using freshly harvested endothelial cells, **we now propose** to determine directly whether 6 weeks of mild sleep restriction, which mimics life-like conditions, increases oxidative stress and inflammation while reducing NO bioavailability in the endothelium of pre- and post-menopausal women (**Aim 1**), to quantify the effects of sleep restriction on the rate of endothelial apoptosis and repair capacity (**Aim 2**), and to identify distinct molecular pathways that promote endothelial dysfunction in SR **(Aim 3)**. Taken together, these experiments may advance our understanding of the mechanisms that mediate increased vascular risks associated with sleep restriction and may suggest novel educational and/or pharmacological approaches for treatment of vascular complications of sleep restriction. Considering that the magnitude of endothelial impairment observed after sleep restriction using indirect assessment of endothelial function is similar to that reported in smoking and diabetes, the potential public health impact of the proposed studies is likely to be significant given the high prevalence of voluntary sleep restriction among American women.