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WOMEN'S HEALTH

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Editorial Note:

Dear Doctor,

It's our immense pleasure to inform you that we have published our newsletter, "Women's Health". In this issue we are focusing on Challenges in managing vaginal prolapse and Predicting cardiovascular disease: risk scoring in women.

Your comments and suggestions will encourage us for upcoming issues. Please participate in quiz competition and win prizes.

Challenges in managing vaginal prolapse

Predicting cardiovascular disease: risk scoring in women

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WOMEN'S HEALTH

Challenges in Managing Vaginal Prolapse

Vaginal prolapse is a common health problem and although severe morbidity is rare, it can have marked effects on quality of life. In general, "vaginal prolapse" includes multiple categories of pelvic support problems, such as uterine prolapse, post hysterectomy vaginal vault prolapse (enterocele), anterior vaginal wall prolapse (cystocele) and posterior vaginal wall prolapse (rectocele). These various support defects can occur in isolation or in combination with one another. The etiology is multifactorial and includes known risk factors of pregnancy and childbirth, increasing age, obesity, hysterectomy, connective tissue abnormalities and conditions associated with increased abdominal strain. Despite potential bother and associated symptoms, not all women with prolapse are symptomatic. While there is no obvious anatomic threshold that correlates with bothersome symptoms, the hymenal remnant seems to be an important landmark, as prolapse symptoms increase with descent to or beyond this level. Women who are asymptomatic from their prolapse do not require treatment and can continue under observation. However, women who are symptomatic have multiple treatment options which include expectant management, the use of a pessary device, or pelvic surgery. Those who are not able to retain a pessary, surgery may be the only treatment option. Ultimately, decisions about treatment tend to be based on the magnitude of symptoms and impact on a woman's quality of life. Thus, for women who choose surgery, physicians are often challenged to not only restore anatomy but also to find treatment choices that result in positive impact on both symptom burden and quality of life.

Selection of Surgical Procedure : The treatment of vaginal vault prolapse can be a difficult and challenging problem. A detailed history and clinical evaluation is required in order to plan the appropriate choice of procedure. There are numerous surgical procedures that are in practice using either abdominal or vaginal approaches. For women with prolapse, one of the biggest clinical challenges is selecting which surgery to perform. In addition to the route of surgery, it should be decided on whether a native-tissue or graft-augmented repair is preferable. If a graft-augmented repair is chosen, there may be choices of different biologic grafts and synthetic mesh materials. Since there are risks and benefits to an approach, surgical counselling requires comprehensive knowledge of types of procedures, as well as the rates of prolapse recurrence and adverse events for each procedure.

Table 1: Characteristics of surgical procedures for prolapse repair

Procedure	Description	Indication	Success rates	Other considerations
Posterior colporrhaphy	Either native-tissue suture repair or graft-augmented repair via vaginal approach; can be midline plication or site-specific defect repair	Repair of rectocele or perineocele	86%-93%	• No data to support benefit from using synthetic mesh or biologic graft augmentation
Anterior colporrhaphy	Either native-tissue suture repair or graft-augmented repair via vaginal approach	Repair of cystocele	40%-88%	• Apical defects often coincide with anterior defects • Anterior compartment is area most prone to recurrent prolapse • Synthetic mesh or biologic graft reduces risk of recurrent cystocele, however increased risk of blood loss, longer operating time, apical and posterior prolapse recurrence, de novo stress, incontinence and carries 11.4% risk of mesh erosion
Sacrospinous ligament suspension	Native-tissue repair via vaginal approach using delayed absorbable and/or permanent sutures to affix the apex of the vagina to the sacrospinous ligament(s) (retroperitoneal)	Repair of apical prolapse, either post-hysterectomy or with uterus in situ	73%	• Pudendal neurovascular bundle close in proximity to ischial spine
Uterosacral ligament suspension	Native-tissue repair via vaginal approach using delayed absorbable and/or permanent sutures to affix the apex of the vagina to the uterosacral ligament(s) (intraperitoneal)	Repair of apical prolapse, post-hysterectomy (prior or concurrent)	70%-75%	• Risk of ureteral injury 1%-2% and risk of neuropathic sciatic-type pain 7%
Abdominal sacrocolpopexy	Open or minimally invasive abdominal approach for suspending vaginal apex to the anterior longitudinal ligament of the sacrum using synthetic mesh or biologic graft	Repair of apical prolapse, post-hysterectomy (prior or concurrent); could also be performed with uterus in situ (sacrohysteropexy)	75%-100%	• Minimally invasive approach with longer operating times but shorter hospital stays and less blood loss with similar anatomic outcomes compared to the open abdominal approach • Mesh erosion risk 3.4%–10.5% • Polypropylene mesh with best anatomic outcomes
Vaginal vault suspension with transvaginal mesh	Transvaginal repair using either trocar-based kits or suture techniques to place synthetic mesh or biologic graft	Repair of apical prolapse, either post-hysterectomy or with uterus in situ	Variable based upon kit or technique used, but generally improved anatomic outcomes	• Improved anatomic outcomes, however no differences in symptoms or quality of life • Mesh-exposure rates vary based upon kit and technique used (0%–29.7%)
Colpectomy/ colpocleisis	Native-tissue repair using sutures to obliterate the internal vaginal length via vaginal approach	Repair of apical prolapse, either post-hysterectomy or with uterus in situ	90%-95%	• Not appropriate for women wishing to retain option for vaginal intercourse

The decision for surgery for prolapse begins with a thorough examination. Severity can be measured with a quantitative pelvic exam, measuring the descent of the individual vaginal walls in the anterior, posterior and apical compartments. The Baden-Walker halfway system and the POP quantitative system (POP-Q) are two common methods of assessing anatomic prolapse. The POP-Q examination is commonly used in research studies due to high reliability and standard classification of prolapse. A standard quantitative exam is important, because it allows the surgeon to individually assess each wall of the vagina for prolapse and in particular allows the surgeon to assess for the degree of apical prolapse. Women may have isolated anterior wall prolapse (cystocele), isolated posterior wall prolapse (rectocele) or may have a combination that also includes apical compartment prolapse (uterine prolapse or enterocele). If an apical defect is noted at the time of initial examination, it is important to include correction of the apex at the time of surgery, as this is highly associated with durability of the surgical repair.

Surgical options may include isolated anterior or posterior vaginal wall repair if these are the only notable defects in support. For women who also have apical prolapse and are not sexually active, surgical options may include obliterative procedures, such as colpectomy/colpocleisis or LeFort colpocleisis. These procedures effectively close off the internal vaginal length and thus preclude future vaginal intercourse, but are also very durable repairs. For women with a component of apical prolapse who are sexually active, reconstructive procedures should be offered, as these procedures provide support while restoring the vaginal contour. Reconstructive surgery for apical prolapse can be performed via vaginal or abdominal routes, and also can be performed entirely using sutures and native tissues or can be augmented with either a synthetic mesh or biologic graft. Choosing between treatment options, particularly surgical options, involves weighing risks and benefits of each type of intervention. In addition to the anatomic location and severity of the prolapse, factors such as the overall health and activity level of the patient and other concurrent pelvic floor symptoms all contribute to the decision of treatment choice.

Isolated posterior compartment defects : In an isolated rectocele without any apical prolapse, surgical decision can be fairly easy. Traditional posterior colporrhaphy uses stitches and the native tissue to re-establish support in the posterior vagina. Recurrence may occur in 7%-14% of women after 1 year. Randomized trials comparing traditional posterior colporrhaphy to biologic graft or synthetic mesh-augmented repairs have shown equivalent or superior anatomic outcomes with traditional posterior colporrhaphy, without the complications associated with grafts. Thus, at this time there are no data to support using mesh or graft augmentation for an isolated posterior compartment defect.

Isolated anterior compartment defects : In women with a presumed isolated cystocele, anterior and apical prolapse are highly correlated and often coexist. If there are co-occurring anterior and apical defects, failure to address the vaginal apex may result in early recurrence of prolapse, regardless of which surgery is performed. Despite the apex of the vagina is well supported and in an isolated anterior compartment defect, there are still some difficult choices regarding surgical repair. The anterior vaginal compartment is the area most prone to prolapse recurrence, with 28%-40% of women experiencing prolapse recurrence after traditional anterior colporrhaphy. Recent data show that a woman's symptoms of vaginal bulge correlate best with success. Thus, a recurrent minor cystocele may be deemed as a “recurrence,” but the patient may be completely asymptomatic with regard to bulge symptoms and perceive her surgery as a “success.” When assessing outcomes after prolapse surgery, anatomy and symptoms are both important, and both should be incorporated into the definition of surgical success. In the anterior compartment there is evidence suggesting that a biologic graft or synthetic mesh may allow for more durability of a surgical repair.

In a recent large systematic review, synthetic mesh or biologic grafts during anterior colporrhaphy were shown to reduce the risk of recurrent cystocele over traditional suture reinforcement alone. Native-tissue anterior colporrhaphy is associated with more recurrent anterior prolapse compared to absorbable polyglactin mesh (relative risk [RR] 1.39, 95% confidence interval [CI] 1.02-1.90) or porcine dermis (RR 2.08, 95% CI 1.08-4.01); however, there were no differences in subjective awareness of prolapse. Native-tissue repairs compared to colporrhaphy with polypropylene (permanent) mesh have an increased risk of recurrent anterior prolapse (RR 3.15, 95% CI 2.50-3.96) and an increased risk of awareness of prolapse (RR 1.57, 95% CI 1.18-2.07). However, in the native-tissue and mesh groups, there were similar rates of reoperation for prolapse and no significant differences in quality of life. Mesh erosion (exposure or extrusion into the vagina) occurs in 11.4% after mesh-augmented anterior vaginal wall repair. Furthermore, mesh repairs are associated with increased blood loss, longer operating time, apical and posterior prolapse recurrences, and de novo stress incontinence. Thus, there are data suggesting that mesh augmentation results in improved anatomic support for anterior wall prolapse, but for women who are choosing surgery to improve quality of life, the potential complications may outweigh the benefits of improved support and durability. For surgeons who are considering a mesh-augmented repair for cystocele, it is important to discuss durability and potential complications, so that the woman can choose the best repair, based on her priorities.

Apical compartment defects : An apical compartment defect, either alone or in combination with other support defects, surgical decision making becomes even more complex. For non-sexually active women, obliterative surgeries may offer the best durability, and are associated with very high postoperative satisfaction and quality of life. However, for the numerous women who wish to remain sexually active, reconstructive surgeries should be offered. These surgeries may involve native-tissue repairs, biologic graft-augmented repairs, or synthetic mesh-augmented repairs, and could be performed from an abdominal or vaginal approach. Thus, there are many options to consider. Traditional surgical procedures for apical prolapse, including native-tissue repairs and abdominal

sacrocolpopexyas well as other less invasive mesh-augmented repairs, such as minimally invasive sacrocolpopexy and transvaginal mesh can be the options.

Native-tissue apical repairs : Though many variations of apical native-tissue prolapse repairs exist, two very common procedures are the sacrospinous ligament fixation and the uterosacral ligament suspension. These procedures involve using delayed absorbable and/or permanent sutures to affix the apex of the vagina to pelvic ligaments. Sacrospinous ligament fixation (SSLF) anchors the vaginal apex to the sacrospinous ligament, and does not require intraperitoneal entry. Thus, it can be performed after hysterectomy or while leaving the uterus in situ. Recurrence of prolapse after SSLF varies based on the outcome definitions that are used, but occurs in up to 27% of women. Uterosacral ligament suspension (USLS) is performed in a transperitoneal fashion and is often performed vaginally after a hysterectomy has already been performed. USLS can also be accomplished laparoscopically, but data are lacking regarding long-term outcomes after the laparoscopic approach. For vaginal USLS, prolapse may recur in 25%-30% of women. The benefit of USLS is that it restores the vagina to its usual axis without involving a permanent mesh implant. Both SSLF and USLS have a similar (25%) risk of recurrent prolapse. There has been only one randomized controlled trial comparing these two native-tissue repairs (SSLF and USLS) and data regarding long-term prolapse recurrence are still being collected. Based on available data, it can't be concluded which among these two procedures may be superior, and the decision on whether to perform SSLF or USLS is based on surgeon preference.

Abdominal sacrocolpopexy : Abdominal sacrocolpopexy (ASC) is a surgical technique for correction of apical and/or advanced anterior wall prolapse that is performed with graft augmentation. Estimates for prolapse recurrence after ASC range from 0% to 22%. This wide variation could be attributed to variability in graft materials. However, even when using synthetic mesh, recent data have challenged the durability of the ASC procedure, showing approximately 25% anatomic prolapse recurrence when patients were evaluated after 7 years. Options for graft augmentation include synthetic mesh materials, such as permanent mesh (woven polyester, polypropylene or expanded polytetrafluoroethylene, [ePTFE]). In addition, there are biologic materials, including xenografts (porcine dermis or bovine tissues) and allografts such as cadaveric fascia. When compared to native-tissue vaginal vault repairs, ASC has demonstrated more durability in multiple randomized trials. The benefits in durability of ASC must also be weighed against longer operating times, longer recovery and potential mesh complications. Since prolapse surgery is offered to improve quality of life, when offering ASC it is important to consider that it may be a more durable approach, but may also require repeat surgery for mesh issues in up to 5%-10% of patients. This is in addition to the 5%-10% of patients who require pessary or surgery for a recurrent bulge. Many women consider repeat treatment for prolapse and repeat treatment for mesh complications to have similar impingement on their quality of life. Thus, when considering whether or not to perform a native-tissue repair or a mesh-augmented repair like ASC, it may be more accurate to weigh the risk of repeat treatment for any reason when counselling the patient.

Minimally invasive sacrocolpopexy : Though ASC is more durable than native-tissue vaginal repair; open abdominal surgery is also more morbid. Laparoscopy, both with and without robotic assistance, has been used to provide mesh sacrocolpopexy without an open abdominal incision. Though operating times are still longer than vaginal surgery, multiple studies of minimally invasive surgery, including laparoscopic sacrocolpopexy (LSC) and robotic sacrocolpopexy (RSC), show shorter hospital stays and less blood loss compared to the open abdominal approach. Even for those who adopt minimally invasive sacrocolpopexy, there is an ongoing debate about whether traditional laparoscopy or robotic-assisted laparoscopy should be used for this procedure. One randomized trial of LSC versus RSC showed no difference in anatomic prolapse or bulge symptoms 1 year after surgery, demonstrating that long-term outcomes after these two minimally invasive approaches may be similar.

Transvaginal mesh : Transvaginal mesh repairs is another approach to provide the benefits of a mesh-augmented repair with a less invasive approach. A recent study of a large US health care showed that, the rate of all procedures for prolapse using mesh grafts increased, with vaginal mesh surgeries constituting the vast majority (approximately 75%). In 2011, a systematic review noted concern that, erosion of mesh through the vagina was a consistent and common mesh-related complication and mesh contraction (shrinkage) was a previously unidentified risk of transvaginal mesh repairs. These complications may lead to pelvic pain, dyspareunia, or the inability to achieve vaginal intercourse. Notably, the review did not find conclusive evidence that transvaginally placed mesh improves outcomes any more than traditional prolapse repair without mesh and may expose patients to greater risk. It is recommended that mesh surgery should be chosen only after weighing the risks and benefits against other alternatives. Mesh augmentation aids in durability of prolapse repair, but it is essential also to minimize complications. Therefore, researches are focusing in investigating the optimal materials for mesh or graft augmentation that would maintain a long-lasting and durable prolapse repair, while minimizing risk of erosion through the vaginal tissue or surrounding organs.

Conclusion : Treatment of POP is clinically challenging because of the need to address pelvic floor symptoms, provide a high quality of life and minimize complications. There is a wide range of surgical options that may be used. The surgeon who treats prolapse should be able to discuss and offer native-tissue procedures for prolapse. In addition, for clinically challenging situations or women with recurrent prolapse, mesh-augmented repairs may be considered. A thorough knowledge of mesh and graft options, as well as knowledge of prolapse recurrence and adverse event rates, can help guide clinicians in counselling their patients effectively. Ultimately, this will allow surgeons to choose personalized treatment options that best align with a woman's lifestyle and treatment goals.

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Predicting Cardiovascular Disease: Risk Scoring in Women

Cardiovascular disease (CVD) is the leading cause of death in both women and men worldwide and a major cause of morbidity. According to the Global Burden of Disease, in 2004, CVD caused almost 32% of deaths in women worldwide vs. 27% in men. With the ageing of the population and because of women's longer life expectancy than men, the proportion of persons, particularly women, who will die of CVD is expected to rise even further in the upcoming decades. CVD risk can be quantified by risk score models using multiple variables and their interactions. This is a cost effective approach to identify high-risk individuals for preventive treatment, especially in Asian countries experiencing large increases in CVD incidence.

Modifiable risk factors associated with CVD and other non-communicable diseases are becoming more prevalent. Although elevated CVD risk factors increase the risk of developing CVD across all ethnic groups, there is emerging evidence of variation in the distribution of modifiable risk factors between ethnic groups which may explain the differences in CVD risk.

The prevalence of risk factors differs across ethnic groups. The rate of hypertension is approximately two times higher in South Asians when compared to the general population of London. In the Asia Pacific Cohort Studies Collaboration study, systolic blood pressure (SBP) and total cholesterol were more strongly associated with CVD risk in Asian than in Caucasian women. Diabetes is also more prevalent in Asian populations consisting of Chinese, Indians and Japanese when compared to Caucasians. The prevalence of diabetes is about six times higher in South Asians when compared to Europeans and should be included in screening and surveys, particularly, in the prediction of CVD risk in Asians. The effect of risk factors on CVD risk also differs in Caucasian and Asian women. For example, when assessing abdominal obesity, a waist circumference (WC) of ≥88 cm would increase a Caucasian woman's risk of diabetes and CVD while a lower cut-off value of WC ≥80 cm would place an Asian woman at increased risk. It should also be noted that results differ depending on which anthropometric measurement is used for assessing adiposity. Bangladeshi women reported a lower prevalence of overweight and obesity (body mass index [BMI] >25 kg/m^2) using BMI but a higher prevalence of raised waist-to-hip ratio (WHR) and WC when compared to the general population of England.

Risk factors

Traditional Risk Factors : As shown by the INTERHEART study, risk estimates associated with traditional cardiovascular risk factors are overall similar in women and men and across various regions of the world. However, the increased risk associated with hypertension and diabetes and the protective effect of exercise and alcohol appear to be somewhat larger in women than in men. Collectively, nine potentially modifiable risk factors (smoking, hypertension, diabetes, waist/hip ratio, dietary patterns, physical activity, consumption of alcohol, plasma apolipoproteins and psychosocial factors) account for 94% of the population attributable risk of AMI in women and 90% in men. For young women with favourable levels of all five major risk factors (smoking, hypertension, diabetes, serum cholesterol and body mass index), IHD and CVD are rare events.

Smoking : Smoking is the single most important preventable cause of IHD in women and the leading cause of IHD in women younger than 50 years old. There is a dose-dependent relationship between total cigarettes consumption per day and risk of AMI; as few as one to five cigarettes per day increase a patient's risk. There is also a well-established increased risk of venous thrombosis and IHD for women who both smoke and use oral contraceptives. After cessation of smoking, the risk of IHD in both women and men declines rapidly (within months) and falls to the level of the risk among non-smokers within 5-10 years. Exposure to passive smoking is also a risk factor for IHD in women, increasing their risk of 24% (22% in men). Although the prevalence of smoking is still slightly higher in men than in women, the decline in tobacco use in recent decades has been less pronounced in women than in men.

Hypertension : For women, as for men, hypertension is a major cause of IHD, as well as of congestive heart failure and stroke. In the INTERHEART study, the risk of AMI in female could be reduced by 36% where hypertension was eliminated as a risk factor. The corresponding figure in men was 19%. Hypertension is two to three times more common in women taking oral contraceptives, especially among obese and older women, than in women not taking them. In older women, isolated systolic hypertension is the most common form of hypertension. A three-fold increase in IHD and stroke is found in women with a systolic blood pressure >185 mmHg when compared with women with a level of <135 mmHg. Control of any form of hypertension has been demonstrated to reduce the risk of IHD and stroke in both sexes.

Dyslipidaemia : Although women aged 20-50 years tend to have more favourable lipid profiles than men, after the onset of menopause cholesterol levels increase in women, whereas they remain steady in men. Reduced HDL cholesterol and high triglyceride levels appear to be more important risk factors in women than in men. HDL cholesterol inversely predicts IHD in both middle-aged and older women, whereas it does not in older men. Among 32826 post-menopausal women from the Nurses' Health Study, HDL cholesterol was the lipid parameter that best discriminated the risk of IHD. Hypertriglyceridemia, on the other hand, is associated with 37% increased CVD risk in women, independent of other risk factors including HDL cholesterol; the corresponding estimate for men is 14%.

Type 2 diabetes : Diabetes mellitus is a major risk factor for IHD for both men and women and among women, it nullifies the female protection towards developing IHD compared with men. Although diabetes has often been associated with a higher IHD risk in women than in men, this is in part due to a higher rate of coexisting risk factors in women with diabetes and to the better survival (relative to men) of women without diabetes. The mortality rates of women with diabetes are actually similar or less, that of men with diabetes. These statistics, however, may be worsening. CVD mortality reductions in the past 30 years have been achieved for diabetic men but not for diabetic women.

Obesity : Obesity is an important risk factor for diabetes and CVD. It is found in 33% of women (and 31% of men), including 7% women (3% men) being extremely obese, defined as a body mass index of ≥ 40. There is a gradient of coronary risk with increasing overweight, with the heaviest category of women having a four-fold increased risk for CVD compared with lean women. Polycystic ovary syndrome is found in 10-13% of women but is often unrecognized; it is linked with a clustering of risk factors, including obesity and type 2 diabetes mellitus, and increased IHD risk after menopause.

Novel biomarkers : A recent summary of systematic reviews conducted for the United States Preventive Services Task Force has reviewed the evidence concerning nine novel risk factors: C-reactive protein, coronary artery calcium score as measured by electron-beam computed tomography, lipoprotein(a) level, homocysteine level, leucocyte count, fasting blood glucose, periodontal disease, ankle-brachial index, and carotid intima-media thickness. However, the review concluded that current evidence does not support the routine use of any of the nine risk factors for screening and risk stratification of intermediate-risk persons. Of the risk markers evaluated, C-reactive protein was the best candidate for screening; nevertheless, evidence is still lacking to recommend routine use.

Risk scores for IHD : The best-known risk algorithm for IHD for asymptomatic persons is the Framingham Risk Score (FRS), which includes age, hypertension, smoking, diabetes and hyperlipidaemia. Many other risk scores have been proposed that have mostly included the same traditional risk factors, but have occasionally added other factors such as family history, measures of social deprivation or new biomarkers such as C-reactive protein. Some of the scoring systems developed in European countries include the SCORE (Systematic Coronary Risk Evaluation), the ASSIGN (Assessing Cardiovascular Risk to Scottish Intercollegiate Guidelines Network/SIGN to Assign Preventative Treatment) and the QRISK (QRESEARCH cardiovascular risk algorithm). A risk score that has been developed specifically for women is the Reynolds Risk Score, whose main difference from the FRS is the incorporation of parental history of IHD and C-reactive protein. This score reclassified 15% of intermediate-risk women (as in FRS) to high risk in the Women's Health Study.

Psychosocial risk factors : There is growing evidence that psychological stress can influence the onset and clinical course of IHD and this may be especially true for women. In the INTERHEART study, the combined exposure to psychosocial risk factors including depression, perceived stress at home or work, low locus of control and major life events was significantly associated with AMI with an adjusted odds ratio (OR) of 2.6 in men and 3.5 in women. Individually, each of these factors predicted AMI in a fairly similar fashion in both men and women.

Depression is about two-fold more prevalent in women than in men; it is especially common, up to 40%, in younger women with AMI. Depression is one of the strongest predictors of non-adherence to medical treatment and an important correlate of lifestyle behaviours such as smoking and sedentary lifestyle. Factors such as anxiety, marital stress, and exposure to early life adversities have been linked to cardiovascular risk in women. On the basis of a recent meta-analysis, anxiety is a moderate but independent risk factor for incident IHD and cardiac death in both men and women, although individual study results are heterogeneous. Acute psychological factors such as stressful events, acute anger, sudden mood disturbances, and extreme excitement can trigger AMI and sudden cardiac death in susceptible individuals. Although it is unknown whether there are sex differences in these effects, a stress-induced condition known as 'takotsubo cardiomyopathy' is almost exclusively seen among women. It manifests as severe, reversible left ventricular dysfunction, with markedly elevated levels of plasma catecholamines.

Unfortunately, psychological interventions aimed at reducing stress or treating depression or other psychosocial risk factors have shown little to no effect on IHD incidence and total or cardiac mortality, although they do achieve small reductions in anxiety and depression in patients with IHD. When results are reported separately by sex, men show a borderline statistically significant benefit [OR 0.73, 95% confidence interval (CI) 0.51-1.05], whereas in women, the estimate is null (OR 1.01, 95% CI 0.46-2.23). However, a recent study documented a remarkable decrease in mortality (about 70% lower) in women with IHD randomized to a stress-reduction intervention specifically tailored to women, compared with usual care. Although promising, the efficacy of such intervention needs to be confirmed in other studies.

Role of sex hormones : The lower incidence of CVD in premenopausal women compared with men of similar age and the menopause-associated increase in CVD have long suggested that ovarian hormones underlie a protective effect on the cardiovascular system for women. Indeed, sex steroid hormones exert multiple direct and indirect effects on cardiovascular physiology. Up to now, research has focused on the effects of oestrogen and oestrogen receptors (ERs), whereas other hormones, such as progesterone and testosterone and their receptors (PR and AR), have received much less consideration.

Cardiovascular effects of oestrogens : Oestrogens improve the arterial wall response to injury and inhibit the development of atherosclerosis by promoting re-endothelialization, inhibiting smooth muscle cell proliferation and matrix deposition following vascular injury. Oestrogens also decrease systemic vascular resistance, improve coronary and peripheral endothelial function, and prevent coronary artery spasm in women with and without coronary atherosclerosis. Interestingly, intracoronary infusion of oestradiol improves endothelial function and coronary blood flow in female patients, but not in male patients with coronary artery disease. Most of the data on the cardiovascular effects of oestrogens relate to vascular function. Much less is known about oestrogens effects on the myocardium. In addition to oestrogens, progesterone may also contribute to sex-specific differences in the regulation of vascular function; its effects, however, remain controversial. Testosterone, on the other hand, was shown to have adverse effects on blood pressure and cardiovascular morbidity and mortality.

Post-menopausal hormone therapy : Given the many potentially beneficial effects of oestrogens on cardiovascular physiology, much expectation was placed on the protective effects of post-menopausal hormone therapy for CVD prevention in women. Initial observational studies did show a reduced incidence of CVD in post-menopausal women using hormone therapy compared with non-users. However, it has recently become clear that hormone therapy has complex biological effects, e.g. it has both anti-inflammatory and pro-inflammatory effects and it both activates coagulation and improves fibrinolysis. Effects depend on many factors, including route of administration, doses of oestrogens and age of the women, among others. Given orally, hormone therapy clearly increases C-reactive protein.

The Heart and Estrogen/Progestin Replacement Study (HERS), and the Women's Health Initiative (WHI) clinical trials did not support beneficial effects of hormone therapy in post-menopausal women, neither in secondary nor in primary cardiovascular prevention. In fact, the WHI study was terminated early due to a small but significant increase in cardiovascular events and other adverse outcomes in the hormone therapy group. In trying to explain these unexpected results, it has been argued that the timing of initiation of hormone therapy after the onset of menopause may influence the response to treatment for CVD prevention. Post hoc analyses of the WHI trial suggested that the CVD risk may be decreased when oestrogen only therapy is started earlier, within 10 years of menopause, but results were not statistically significant. For the combination of oestrogen and progestin therapy, there was no indication of a decreased CVD even among women who initiated therapy within 10 years after menopause; a possible cardioprotective effect in these women became apparent only after 6 years of use. Because the typical duration of hormone therapy is <10 years, most women considering combined oestrogen plus progestin therapy for the relief of menopausal symptoms should not expect protection against CVD. Thus, no trial of hormone therapy has conclusively demonstrated a beneficial effect towards CVD in either primary or secondary prevention; if anything, risk is slightly increased. Therefore, hormone therapy should not be used for the prevention of CVD in women.

Conclusions

Women largely share similar cardiovascular risk factors for IHD with men; however, there are important sex differences in the prevalence of coronary atherosclerosis and coronary vascular physiology with relevance to IHD risk. Differences in epidemiology may reflect important aspects of cardiovascular pathophysiology that differ between the sexes. Eventually, a better understanding of these processes may improve the clinical management of IHD in women, because it may help to devise new strategies for the prevention, detection and treatment of IHD that are better tailored to women.

Reference: Cardiovasc Res. 2011 Apr 1;90(1):9-17.

Congratulations !

The Winners of WOMEN'S HEALTH *Quiz Competition*

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Dr. Nilufa Jahan
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