



Erectile dysfunction and testosterone screening with prostate specific antigen screening at age 40: are these three gender specific determinants additive for overall men's health and do they improve traditional non-gender specific determinants to lessen cardiovascular risk and all-cause mortality?

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SUMMARY

Aims: Assess support for a recommendation to add screening for both erectile dysfunction (ED) and hypogonadism to the initial medical evaluation of young-to-middle aged (≥ 40 years of age) men in light of recent guidelines suggesting prostate-specific antigen screening occur at that age. **Methods:** A search of literature published from 1998 to 2009 was performed. Search terms included: ED combined with coronary artery disease (CAD), metabolic syndrome and hypogonadism, hypogonadism and ED, hypogonadism, ED and mortality. Articles were evaluated according to the Center of Evidence-Based Medicine. **Results:** Both retrospective and prospective evaluations have demonstrated a strong relationship between ED, established cardiovascular risk factors, CAD and the potential occurrence of cardiovascular events. Low testosterone levels are associated with ED. Low serum total testosterone is an independent risk factor for both metabolic syndrome and type 2 diabetes and all-cause mortality. **Conclusion:** Traditionally, ED and testosterone levels have been considered mainly, if not exclusively, in the context of sexual health. The results briefly summarised herein and other recent reviews suggest that ED and hypogonadism are signals of future all-cause mortality and overall health status and thus move these evaluations into the broader arena of public health. Screening for ED and hypogonadism provide 'gender-specific determinants' to assess general metabolic and cardiovascular health risks in men. It is the opinion of the authors that this screening be performed in addition to the well-established non-gender-specific screening tests of lipids, blood pressure, obesity and serum glucose.

Introduction

Comprehensive health assessment should become an increasingly important component of general practice (1) and evaluation, and management of risk for cardiovascular disease (CVD) is a key component of this process. Results compiled by the Centers for Disease Control (CDC) indicated that CVD is the number one source of mortality for both men and women in the United States (US), accounting for 615,651 deaths in 2007 (2). The most recent Heart and Stroke Update from the American Heart Association (AHA) indicated that 38.7 million men in the

US have CVD and that there were about 410,000 deaths caused by CVD in US male patients in 2005 (3). While non-gender-specific determinants of physical examination and laboratory tests [e.g. blood pressure; body mass index (BMI) and waist circumference; fasting blood sugar and lipid profile assessments] do provide important information about cardiovascular (CV) risk, a large percentage of patients are asymptomatic prior to the occurrence of potentially life-threatening events, such as myocardial infarction (MI) and stroke (4,5).

While CVD is associated with the presence of traditional risk factors and may be associated with some

Review Criteria

Centers of Evidence Based Medicine: No articles below Level 2.

Message for the Clinic

ED and Testosterone are commonly considered by clinicians to be solely measures of sexual health. We suggest these measures have far greater impact and relationship to all-cause mortality than PSA, the traditional gender-specific marker of disease in men.

of the newer biomarkers, it is also associated with the presence of metabolic syndrome. It has become clear that ED precedes CVD by 2–3 years (12). This correlation suggests that the risk assessment of the patient with ED may be broadened to include measurement of markers associated with metabolic syndrome: elevated blood pressure; increased waist circumference; glucose intolerance; elevated triglycerides and low HDL cholesterol. This broader assessment of risk leads to the concept of 'cardiometabolic' risk as opposed to pure cardiovascular risk.

Cardiometabolic risk entails the risk of developing any one of the following: type 2 diabetes, CVD or metabolic syndrome. The assessment of cardiometabolic risk uses the classical risk factors such as smoking, high LDL-C cholesterol, hypertension and an elevated serum glucose as well as emerging risk factors closely related to abdominal obesity, especially intra-abdominal or visceral obesity.

Current guidelines for management of elevated lipids are based on the underlying degree of cardiovascular risk. An optimal lipid panel would include the following values: LDL levels < 70 mg/dl (in individuals classified as very high risk), HDL levels \geq 40 mg/dl, triglycerides < 150 mg/dl and total cholesterol < 200 mg/dl (6). Given the evidence that many men with ED have clinical vascular disease, it seems reasonable for physicians to consider managing men with ED to optimal fasting lipid levels. Data from the Heart Protection Study (7) and the ASCOT-LLA study (8) historically have shown the clear benefits of aggressive lipid lowering in men considered at increased risk for developing CVD. These benefits were seen despite the fact that their lipid levels were unremarkable.

The difficulty in assessing risk for CV events is underscored by the recommendation from the Screening for Heart Attack Prevention and Education Task Force that all men aged 45–75, except for those at very low risk, undergo non-invasive atherosclerosis imaging (9). While clinical results support this recommendation, the associated costs do make it difficult to implement. However, the cost of screening for the presence of erectile dysfunction (ED) in men with a validated instrument such as the SHIM-5 is nominal (10). Our belief is for those clinicians who wish to employ gender-specific markers of health prevention begin first with screening for sexual dysfunction in men. If these clinicians choose to screen for sexual dysfunction, then in light of the cardiometabolic comorbidities, it is plausible to add testosterone to this examination. If testosterone screening is implemented, then prostate-specific antigen (PSA) screening is justified by

all accepted guidelines noting the management of testosterone deficiency.

The American Urologic Association (AUA) now recommends baseline screening for PSA in men 40 years of age with an anticipated lifespan \geq 10 years to establish a baseline for future test results (11). While this recommendation is certainly important for the early detection and intervention, if appropriate, of prostate cancer (PCA), and perhaps chemoprevention if the individual is at risk of PCA, we acknowledge that this is an area of tremendous evolution and controversy in terms of noting overall reduction in morbidity and mortality. It is also the most common gender-specific screening test utilised by primary care clinicians in their evaluation of middle and older aged men, although these patterns will perhaps change with further data. It is the authors' opinions that screening for PSA remains of value for age-appropriate risk-stratification for PCA, and is also necessary when utilising testosterone as a screening measure of a man's metabolic health. If one draws a serum testosterone, then one must be prepared to measure and follow serum PSA.

ED as the primary gender-based screening evaluation for health status of men

In his landmark 2005 report of over 9400 men, Thompson et al. (12) pose the following questions: 'With the high prevalence of erectile dysfunction (ED) in aging men, do pharmacologic, lifestyle, or behavioural interventions that are cardioprotective also reduce or delay onset of erectile dysfunction? Could erectile dysfunction serve as a surrogate measure of treatment efficacy in preventive interventions for cardiac disease?' Today, 5 years later, while these questions remain unanswered, newer data have sought to clarify the issue.

In the study by Thompson et al. (12) as part of the Prostate Cancer Prevention Trial, men aged 55 years and older who were included in the placebo group ($n = 9457$) were evaluated at 3-month intervals for ED and subsequent CVD. There were 4247 men with no ED at study entry; 2420 developed incident ED (defined as the first report of ED of any grade) over 5 years. Incident ED (adjusted for other cardiovascular risk factors) was associated with a hazard ratio (HR) of 1.25 [95% confidence interval (CI) 1.04–1.53; $p = 0.04$] for subsequent cardiovascular events including MI, coronary revascularisation, cerebrovascular accident, transient ischemic attack, congestive heart failure, fatal cardiac arrest or non-fatal cardiac arrhythmia. The adjusted HR was even higher (1.45; 95% CI 1.25–1.69; $p < 0.001$) for men with either incident or prevalent ED (i.e. ED at study entry). Therefore, the authors concluded that inci-

dent ED had an effect equal to or greater than the effects of family history of MI, cigarette smoking or measures of hyperlipidaemia on subsequent cardiovascular events (12).

If a man presents with ED, then draw a serum T

Whether or not low testosterone levels are an independent risk factor for CVD is less clear. Results from the Tromso study indicated that men in the lowest quartile for free testosterone had significant increase for all-cause mortality, but not for first ever MI (13). A population-based cohort study of 1709 men (40–70 years of age) followed up for 15.3 years indicated that low free testosterone was also associated with significantly increased risk for respiratory mortality ($p = 0.002$) (14). Results from the European Prospective Investigation into Cancer in Norfolk indicated that lower testosterone levels were associated with increased risk for all-cause ($p < 0.001$) and CV ($p < 0.01$) mortality (15). A study of 858 military veterans > 40 years of age also showed that lower testosterone levels were significantly associated with increased all-cause mortality, 34.9% vs. 20.1% mortality incidence in those men termed eugonadal ($p < 0.05$ based on 95% CI's) (16).

This review focuses firstly on assessment of ED as a marker for CV events; and the benefits of ED screening with a simple instrument, such as the Sexual Health Inventory for Men (SHIM)-5, to identify patients who may have high risk for CVD. Just as ED is a marker of CV events, a growing body of the literature has also indicated a strong correlation between low serum testosterone and increased mortality risk in middle-aged men in addition to a strong association with metabolic syndrome and type 2 diabetes. Therefore, we also suggest that serum total testosterone be the second gender-specific determinant drawn in addition to the ED evaluation, and if testosterone is utilised, then serum PSA in 40-year-old men and older must be considered the third gender-specific determinant at their initial health surveillance examination if we are to utilise testosterone repletion.

Erectile dysfunction and CVD

Results from both retrospective and prospective evaluations have demonstrated a strong relationship between ED, established CV risk factors, coronary artery disease (CAD) and the occurrence of CV events. Analysis of a managed care claims database that covered 51 health plans with 28 million lives identified 272,325 men with ED and showed that 68% had a concurrent diagnosis for either hypertension (41.6%), dyslipidaemia (42.4%), diabetes mell-

itus (20.2%) or depression (11.1%) (17). The age distribution of all patients with ED was 5% (18–35 years old); 16% (36–45 years old); 72% (46–65 years old) and 7% (> 66 years old). A smaller scale analysis of 154 men with symptoms of ED for ≥ 6 months indicated that 44% had hypertension, 23% had diabetes mellitus, 79% had a BMI $> 26 \text{ kg/m}^2$ and 74% had a low-density lipoprotein cholesterol (LDL-C) level $> 120 \text{ mg/dl}$ (18).

Results from several studies have demonstrated a strong correlation between the presence of ED and CAD. In one of the earliest studies Greenstein et al. assessed erectile function with a questionnaire in 40 patients undergoing coronary angiography. Study results indicated that men with two- or three-vessel disease were significantly more likely than those with single-vessel disease to have difficulty achieving erections ($p < 0.007$) (19). Subsequent studies have demonstrated that the presence of vasculogenic ED is significantly correlated with coronary artery calcification in men with no clinical history of CAD ($p = 0.01$) (20) and that there is a significant correlation ($p < 0.0001$) between ED, as assessed by the International Index of Erectile Function (IIEF) and coronary calcium scores in men with no clinical history of CAD (21). Angiographic assessment of 50 consecutive men with non-psychogenic and non-hormonal ED indicated that 20% had evidence of CAD (22). A study of 575 men without previous CAD who were screened for ED with the IIEF and underwent stress myocardial perfusion single-photon emission computed tomography imaging (MPI) indicated that 46% had ED and that it was associated with adverse prognostic indicators on MPI (23). Results from a similar evaluation of 221 men referred for MPI and evaluated for ED with the IIEF indicated that 54.8% had ED and that it was significantly associated with higher summed stress score ($p < 0.001$) and left ventricular ejection fraction $< 50\%$ ($p = 0.01$). Multivariate analysis of results from this study indicated that ED was a significant independent predictor of coronary heart disease [odds ratio (OR) = 2.50, 95% CI = 1.24–5.04, $p = 0.01$] (24).

The presence of ED is also predictive for the occurrence of coronary heart disease events; and this should not be surprising as the risk factors for CVD and ED are similar. As previously noted in the seminal study by Thompson et al., ED was not only associated with but also predictive of CVD, with the longer the duration of ED more the predictive of CVD events. Results from 9457 men (≥ 55 years of age) who were randomised to placebo in the Prostate Cancer Prevention Trial were used to evaluate the relationship between ED and the occurrence of CV events. At study entry, 85% of the 9457 men rando-

mised to placebo had no CVD and 47% had ED. An additional 25% reported ED during the 5-year study period. Incident ED was significantly associated with risk for CV events (HR = 1.25, 95% CI = 1.02–1.53, $p = 0.04$). For men with either incident or prevalent ED, the HR was 1.45 (95% CI = 1.25–1.69, $p < 0.001$) (12). A more recent population-based study has also indicated a significant correlation between the presence of ED and risk for CV events. A study carried out in a small city in the Netherlands requested participation of all men 50–75 years old, without a history of bladder or PCA, radical prostatectomy or neurogenic bladder disease. Subjects answered a single question on erectile rigidity included in the International Continence Society male sex questionnaire; and baseline CV risk factors, including age, smoking status, blood pressure, total- and high-density lipoprotein cholesterol, and diabetes, were determined and used to calculate Framingham risk scores (25). Patients were followed up for a mean of 6.3 years. Of the 1248 men free of CVD at baseline, 22.8% had reduced erectile rigidity and 8.7% had severely reduced erectile rigidity. In a multiple variable Cox proportional hazards model adjusting for age and CVD risk score, the HR for CV events for men with decreased erectile rigidity was 1.6 (95% CI = 1.2–2.3) and that for men with severely reduced erectile rigidity was 2.6 (95% CI = 1.3–5.2) (25). The study investigators concluded that a single question on erectile rigidity was a significant predictor for the composite end-point of acute MI, stroke and sudden death, independent of those employed to calculate risk with the Framingham equation (25). Most recently, a prospective population-based study of 1709 men (40–70 years old) followed up for 15 years indicated that ED is a significant independent risk factor for all-cause mortality (HR = 1.26, 95% CI = 1.01–1.57) and CV mortality (HR = 1.43, 95% CI = 1.00–2.05) (26).

Does ED contribute to CVD risk prediction beyond Framingham?

Araujo et al. examined 1709 men of age 40–70 and ED data were measured by self-report. Subjects were followed up for 11.7 years. Independent of established risk factors, ED is significantly associated with increased CVD incidence. Nonetheless, ED does not improve the prediction of who will and will not develop CVD beyond that offered by traditional risk factors as indicated by the 10-year Framingham Risk Score (27). However, the National Cholesterol Education Program and the American Heart Association recommend consideration of lifetime risk estimates in primary prevention of CVD but without specific guidance as to incorporate the two risk prediction

scores currently accepted, e.g. the Framingham 10-year risk and the previously published lifetime risk algorithm by Lloyd-Jones et al. (28). They recommend incorporating a stepwise approach to CVS risk stratification with the Framingham criteria used for all patients and the lifetime analysis added for those predicted to be at low 10-year risk. Present screening methodology including the standardised Framingham coronary risk may be misleading for men < 60 years of age. In this most recent study (29), 56% of Americans had a low 10-year risk but a high 'lifetime' risk of a cardiovascular event. Men saw a disproportionate rise in short-term predicted risk with older age, such that after age 60 nearly 90% of men were at high risk. Notably, in the 40–59 age group – of particular interest for clinical prevention – 80% had a low 10-year coronary risk, but three-fourths of them had a high lifetime risk of CVD events. This argues for further cardiovascular workup in the intermediate-risk ED patient.

All of the results summarised in this section indicate that CV risk should be carefully evaluated in men who presents with ED (30). In addition, they suggest further that screening men for ED, even in those for whom other commonly evaluated non-gender-specific risk factors have been evaluated, will provide additional independent information regarding CV risk (25). Screening for ED is also supported by observations indicating that it is often present prior to clinically evident CVD. A recently published study that enrolled 1402 men (40–79 years of age) without evidence of CAD and with regular sexual partners were screened biennially for ED using the Brief Male Sexual Function Inventory (BMSFI) and events indicative of CAD, including sudden cardiac death, MI and angiographically diagnosed coronary disease (31). The prevalence of ED was 2% for men aged 40–49 years, 6% for those 50–59 years old, 17% for men aged 60–69 years, and 39% for men ≥ 70 years of age. The CAD incidence densities per 1000 person-years for men without ED in each age group were 0.94, 5.09, 10.72 and 23.30. For men with ED, they increased to 48.52, 27.15, 23.97 and 29.63, respectively (Figure 1) (31). These results support two important conclusions. First, ED occurs more often than CAD in younger men; and second, it is indicative of increased future risk for cardiac events. By contrast, the presence of ED had little correlation with the occurrence of incident cardiac events in men ≥ 70 years of age (31). A very large-scale survey carried out using the SHIM questionnaire in 9956 men 25–55 years of age indicated that 25.2% had ED. Study results also indicated that 45.2% of the men evaluated had dyslipidaemia and that the risk for ED was twice as high in men with

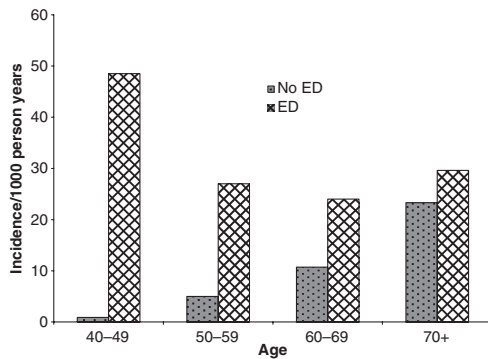


Figure 1 Incidence per 1000 person years of ED associated with CAD Densities (Incidence Densities in patients with and without ED). Inman B. Mayo Clinic Proceed: 2009

diabetes vs. those without this disease ($p < 0.0001$) (32). The same group assessed whether ED, as assessed by the SHIM, might be indicative of poorer prognosis in men with diabetes ≥ 40 years of age. Results from this study indicated that men with diabetes and with or without ED did not differ significantly with respect to mean age, BMI or prevalence of CV risk factors. Therefore, while the issue of prognosis in the diabetic population in those men with vs. without ED is unclear, ED appears to be an independent predictor of CVD in this population.

Gazzaruso et al. (33) recruited 291 type 2 diabetic men with silent CAD and found that those who developed major adverse cardiac events over the course of approximately 4 years were more likely to have ED (61.2%) than those who did not (36.4%). Through further multivariate analysis, ED remained an important predictor of adverse cardiac events, and although diabetics have a high risk of CVD, the risk is even higher in those who develop ED. In addition, in that study, statin use significantly reduced major events. There also was a trend for suggesting that the periodic use of phosphodiesterase type 5 (PDE5) inhibitor drugs was associated with a lower rate of cardiac events. The former observation is not unexpected given the findings of recent large clinical trials such as CARDS (34) and JUPITER (35), each showing a reduction of non-fatal MI and strokes with 10 mg of atorvastatin and 20 mg rosuvastatin, respectively in specific populations (diabetic in the former; elevated highly sensitive C-reactive protein in the latter).

Ma et al. (36) studied 2306 diabetic men with no clinical evidence of CAD, of whom 27% had ED. Over the course of approximately 4 years, the incidence of coronary heart disease was greater in men with ED (19.7/1000 person-years) than in men without ED (9.5/1000 person-years). After adjustments for other covariates, including age, duration of dis-

ease, antihypertensive agents, and albuminuria, ED remained an independent predictor of coronary heart disease (HR 1.58, 95% CI 1.08–2.30, $p = 0.018$).

In a just released study of 1549 patients with CVD, the issue of whether ED is predictive of future events in this subclass of patients was examined. Indeed, ED was found to be a potent predictor of all-cause death and the composite of cardiovascular death, MI, stroke and heart failure in men with CVD (37).

All of these results support the view that assessment of ED can readily identify men with increased CV risk and possibly provide a 'window of curability,' in which progression of cardiac disease in younger men identified by the presence of ED might be slowed or reversed by appropriate intervention (38). 'These data could serve as a basis for preventing life-threatening events by risk factor management and lifestyle modification in men with ED' (39). This remains to be embraced by primary care providers who still largely see ED as a quality of life issue and not as a sentinel marker of cardiovascular events and a competing issue in the rapid evaluation of the highly morbid disease states (e.g. hypertension, diabetes and Chronic Obstructive Pulmonary Disease) that occupy a normal office visit. Because of its nominal cost and strong predictive focus for future CVD events, we maintain that ED should be the first gender-specific determinant utilised to evaluate the middle-aged and older man.

Testosterone level and risk for diabetes and metabolic syndrome

A diabetes epidemic in the US now exists. The most recent estimate from the Centers for Disease Control indicates that 23.6 million people have diabetes and that 24% of these people have not received a formal diagnosis of their condition (40). An additional 25.9% of adults ≥ 20 years of age have impaired fasting glucose (IFG) (40). Individuals with either IFG or diabetes are at increased risk for CV events (41–43). Metabolic syndrome, defined by the National Cholesterol Education Program as the presence of at least three of the following five conditions: abdominal obesity, elevated triglycerides, reduced high-density lipoprotein cholesterol and elevated fasting glucose (IFG or type 2 diabetes) (44) also has a high prevalence (35.1%) of men (45); and is associated with significantly elevated CV risk (46–48).

The presence of diabetes is also associated with increased risk for ED and, as noted above, both conditions are predictive of CVD (49). While these relationships may be attributed in part to shared comorbidities (e.g., hypertension, dyslipidaemia)

(18,50), a growing body of evidence suggests that low testosterone levels may play a key role in all of these conditions. It has been estimated that as many as one-third of men with diabetes have low testosterone concentrations (51); and results from a study of 3156 African American, non-Hispanic white, Hispanic and Chinese-American men (45–84 years of age) indicated that the incidences of both IFG and diabetes were inversely correlated with total testosterone (52). Low testosterone levels are also associated with increased risk for the occurrence of metabolic syndrome (Figure 2) (53–55). Results from a study of 2794 men 25–80 years of age presenting with a primary complaint of ED indicated that 7–47% had androgen deficiency with testosterone levels < 200 to < 400 ng/dl (56).

In a recent population-based cohort of men aged 20–79, Haring et al. (57) examined all-cause and cause-specific mortality in men with low testosterone levels. Although the association of low serum testosterone levels with mortality has gained strength in recent research, there are few population-based studies on this issue. Researchers used data from 1954 men recruited for the prospective population-based Study of Health in Pomerania, with measured serum testosterone levels at baseline and 195 deaths during an average 7.2-year follow up. A total serum testosterone level of < 8.7 nmol/l (250 ng/dl) was classified as low. The relationships of low serum testosterone levels with all-cause and cause-specific mortality were analysed by Cox proportional hazards regression models. Men with low serum testosterone levels had a significantly higher mortality from all causes than men with higher serum testosterone levels (HR 2.24; 95% CI 1.41–3.57) (57). After adjusting for waist circumference, smoking habits, high-risk alcohol use, physical activity, renal insufficiency and

levels of dihydroepiandrosterone sulphate, low serum testosterone levels continued to be associated with increased mortality (HR 2.32; 95% CI 1.38–3.89) (57). In cause-specific analyses, low serum testosterone levels predicted increased risk of death from CVD (HR 2.56; 95% CI 1.15–6.52) and cancer (HR 3.46; 95% CI 1.68–6.68), but not from respiratory diseases or other causes (57). In conclusion, low serum testosterone levels were associated with an increased risk of all-cause mortality independent of numerous risk factors. As serum testosterone levels are inversely related to mortality caused by CVD and cancer, it may be used as a predictive marker. We believe it is the second gender-specific determinant to be employed in the health determination of middle and older aged men.

There is a growing understanding that testosterone deficiency may provide an important link between metabolic syndrome, type 2 diabetes and ED. This interdependence supports the suggestion that assessment of testosterone levels should become routine in men with or without ED. This is in stark contrast to the recently published ACP Guidelines for the management of ED that concluded there is insufficient evidence for or against the use of hormonal testing in the workup of ED (58).

The role of PSA in men's health: the most common gender-specific determinant employed by clinicians

The recommendation of the AUA to suggest PSA screening initially in men at age 40 years (11) was

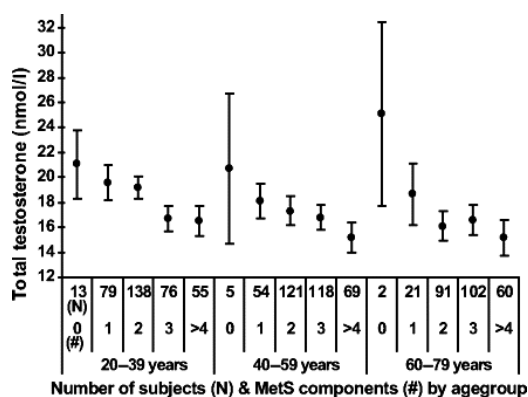


Figure 2 Means with 95% CI in the analytical sample (N = 1004) for total testosterone levels according to zero, one, two, three, four, or more components of metabolic syndrome at baseline by 20-year age-groups (55)

Table 1 Prostate Health Assessment (65)

Prostate Health Assessment

DRE

PSA

Consult with urologist

PSA >4.0 ng/mL

PSA velocity >0.4 ng/mL/y (using PSA level after 6 mo of therapy)

Detection of prostate abnormality on DRE

AUA prostate symptom score >19 with bother if PCP uncomfortable

AUA = American Urological Association.
Braun S et al. J Clin Endocrinol Metab. 2006;91:1995-2010.

AUA, American Urological Association; PSA, prostate-specific antigen; DRE, Digital Rectal Exam; PCP, Primary Care Provider.

suggested despite the conflicting mortality results regarding PSA screening of two seminal studies, the American PLACO study (59) and the European ERS-PC study (60). Although PCA risk correlates with PSA, there is no PSA value below which a man may be reassured that he does not have biopsy-detectable PCA. The AUA advocates for a baseline PSA test at the age of 40 with an anticipated lifespan of 10 or more years, and subsequent rescreeing that encompasses overall risk, baseline PSA, PSA velocity and free and total PSA (11).

It is the author's opinion that PSA be monitored according to Table 1. It is the authors' belief that PCA screening with PSA continues in those men beginning at age 40 years with risk factors including a family history, African American race or simply if a man desires screening after being appropriately informed. The basis for this is that knowledge does not have to translate into active, highly morbid treatment as we are learning to offer active surveillance for localised, low-volume prostate carcinomas. Finally, if one is going to examine the gender-specific determinants of ED and testosterone, then it is the authors' opinion that PSA is a necessary test in the management of these conditions.

Conclusions

Screening for metabolic abnormalities and symptoms that may indicate the presence of or elevated risk for chronic disease has become an integral part of medical practice. At present, the American Urologic Association recommends baseline screening for PSA in men 40 years of age with an anticipated lifespan ≥ 10 years to establish a baseline for future test results while other primary care guidelines recommend the more common non-gender screening tests (61). Although PSA remains highly controversial, the authors feel that this single gender-specific test is insufficient alone to guide the male patient and provider with assessment of cancer mortality and overall cardiometabolic risk. Given the close associations of ED with CVD and of low testosterone with both diabetes and metabolic syndrome, both well-established CVD risk factors, it is reasonable to suggest that ED and testosterone levels should also be evaluated routinely in young and middle-aged men at the same time as the recommended assessment of PSA. Traditionally, ED and testosterone levels have been considered mainly, if not exclusively, in the context of sexual health. The results summarised this article and other recent reviews (62–64) suggest that these measures also provide gender-specific determinants to assess general health in men, including overall CVD risk and mortality risk.

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