screening programs worldwide (Table 1). The complication rate for prostate biopsy (% complication of biopsy) was assumed to be 5.0% according to reports by Berger *et al.*[13] Raaijmakers *et al.*[14] and Carey *et al.*[15] The cost of biopsy and the cost of management of biopsy complications were assumed to be \$150 and \$500, respectively, as reported by Ellison *et al.*[16] and Larsson *et al.*[17] The sensitivity and specificity of conventional PSA were assumed to be 0.95 and 0.10, respectively, based on an excellent review by Roddam *et al.*[6] The prevalence of prostate cancer was assumed to be 0.03 in Thompson's reports[18,19] in addition to the reports on prostate cancer screening programs worldwide (Table 1). In the decision tree model, the probability of a positive primary screening test ($P_{\text{positive primary screening test}}$) was calculated as:

$$P_{\text{positive primary screening test}} = \text{prevalence} \times \text{sensitivity} + (1\text{-prevalence}) \times (1\text{-specificity})$$

Using a two-way sensitivity analysis incorporating the cost and specificity of primary screening tests, isocost curves were plotted as the locus of input combinations of the cost and specificity of the primary screening test along which the total screening cost for a participant remains constant. Each isocost curve was dotted as a straight line since the analysis focused on the cost of a screening program with respect to the cost and specificity of the primary screening test from the viewpoint of introducing a new primary screening test into an existing screening program. The tangential inclination of the isocost curves expressed an impact of 1% improvement in the specificity on the total screening cost as well as a threshold of acceptable cost elevation per 1% improvement in the specificity. This corresponds to the marginal rate of substitution of unit cost of primary screening test for a 1% improvement in the specificity. If the cost elevation in a new test for specificity improvement was lower than the marginal cost elevation, the cost elevation was considered acceptable. This means that the use of the new primary screening test eventually costs less compared to the use of the conventional test when the total screening costs (including primary screening, biopsy and management of biopsy complications) are considered.

Since several of the input parameters estimated from previous reports for this analysis might have been inconclusive, three-way sensitivity analyses were run to test all assumptions of the model by incorporating them in addition to the cost and specificity of the primary screening tests. The decision-analytic model was constructed using TreeAge Pro 2005 software (TreeAge Software, Inc., Williamstown, Massachusetts, USA). As this analysis was designed for a single round of screening, annual discount was not incorporated. Since our perspective is limited to costs for a screening program as a function of test specificity, the cost studied in our model was simply for screening until prostate cancer diagnosis. The consequent costs for staging and treatment in patients diagnosed with prostate cancer in the screening program as well as unrelated medical costs need not be taken into consideration because they do not vary according to changes in the cost and specificity of the primary screening. The societal health burden that is charged by participating in the screening program including informal care such as transportation expenses, impaired quality of life and production loss from work reduction were not considered due to simplicity and data availability.

Results

The overall cancer detection rate, the proportion of cancer cases to the number of all participants, was 2.0% in the base case of the decision-analytic model. The expected cost for each participant was \$111 if the cost of PSA was \$10. The threshold of acceptable cost elevation for a 1% improvement in the specificity for the base case was 1.188 \$/% (Fig. 2a). This means that a 1% improvement in the specificity of the primary screening test provides a 1.188\$ cost saving per participant.

A three-way sensitivity analysis showed that the sensitivity did not influence the threshold of acceptable cost elevation. As shown in Figure 2, biopsy compliance, % complication of biopsy, cost of biopsy, cost of management of biopsy complication and prevalence of prostate cancer influenced the threshold of acceptable cost elevation to various degrees. Acceptable cost elevation varies from 0.679 to 2.207 \$/% according to the changes in the input parameters (Table 3). The influence of biopsy compliance and the cost of biopsy on the threshold of acceptable cost elevation seemed greater than that of the other parameters within the range indicated in Table 3.

Discussion

Outputs from our model including overall cancer detection rate and expected cost per participant are comparable with those of previous reports on the practical screening programs,[7-12] or hypothetical models.[16] It suggests that our model could well express a similar outcome to practical prostate cancer screening programs.

The base case analysis of the decision-analytic model indicated that an impact of 1% improvement in the specificity of the primary screening test is \$1.19 cost reduction per participant. It suggests that only a 1% improvement in the specificity provides over \$ 30 000 of cost reduction in a prostate cancer screening program on a scale of 30 000 participants. If a new primary screening measure that is more expensive by \$5 but more specific by 10% is used, cost reduction will be more than \$150 000. Contrarily, the use of a primary screening test with a specificity lower by 5% will result in a cost increase even if it is lower-priced by \$5. The impact of the specificity improvement on the total cost of a prostate cancer screening program has been rarely analysed using such measures as this study incorporating the cost balance between higher priced primary screening measures and the reduced number of participants who need secondary screening. The study could present an important consideration about the issue using a simple decision-analytic model.

The findings of the study will be helpful when the development and introduction of new primary screening measures are considered. The results of three-way sensitivity analyses in this study indicate that a new test will be more economical in most screening programs if the unit price elevation for a 1% improvement in the specificity is limited to up to \$ 0.50. On the contrary, a new screening measure will become rather expensive if the unit price elevation exceeds \$ 2.5/% even though the measure is more specific. These values are fine targets on the commercialization of a new primary screening measure for prostate cancer detection. From the standpoint of manufacturers developing a more specific assay, for instance, the developmental cost should be limited so that the price elevation does not exceed the acceptable cost elevation for the improved specificity. From the standpoint of promoters of screening programs, a new assay with a 10% advantage in specificity should be adopted even if the test is more expensive by \$5.

There has been little evidence for a comprehensive comparison including the costs and specificity between two primary screening measures and the results of this study would provide significant evidence for the development and selection of primary screening measures. According to a previously reported model by Ellison *et al.*[16] complex PSA is more specific by 0.6% compared to total PSA at almost the same sensitivity levels, and more expensive by \$10. They estimated the total screening cost per participant of the strategy using complex

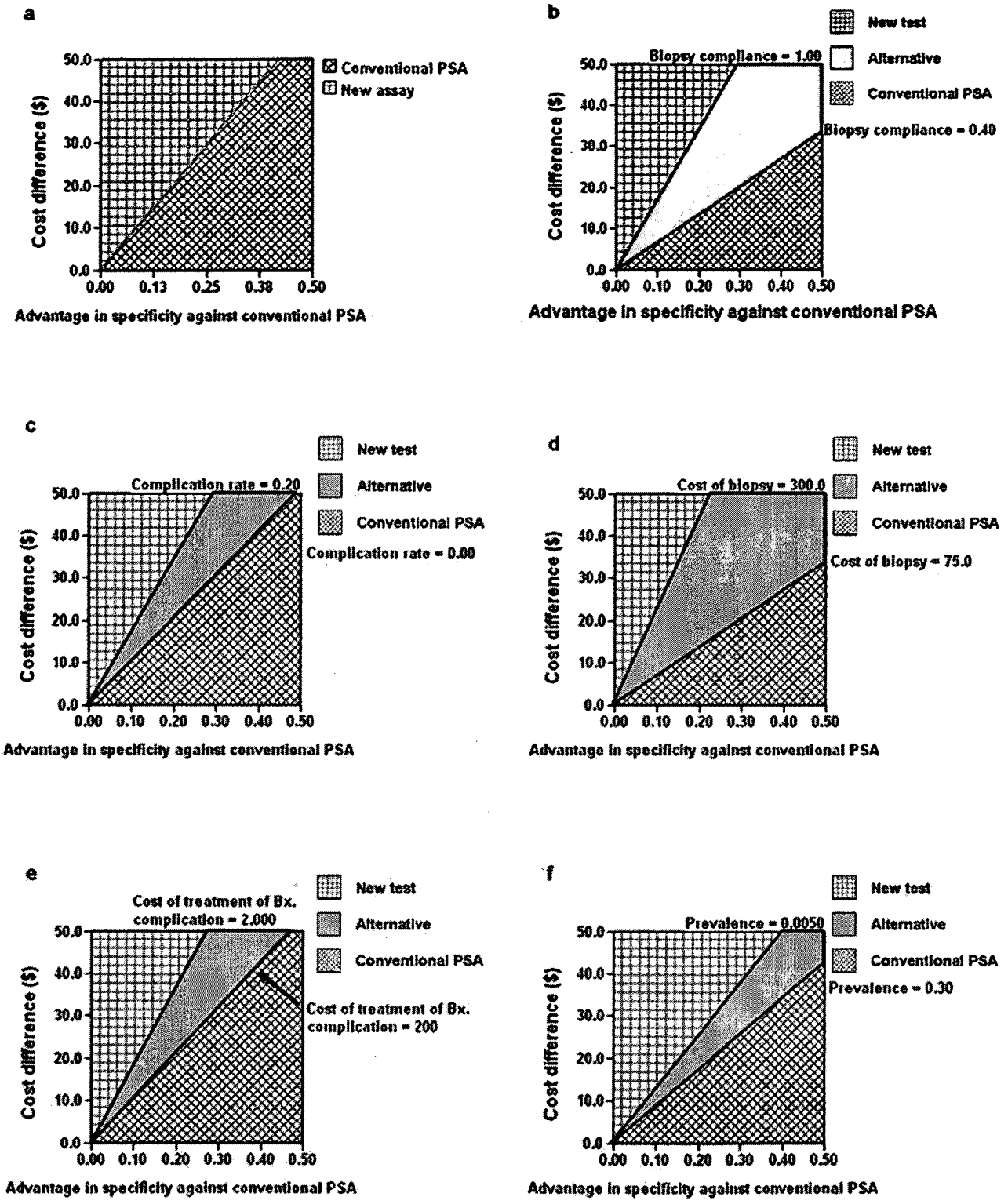

Fig. 2 (a) Two-way sensitivity analysis with regard to differences in the specificity and cost between two primary screening tests in the base case. The inclination of the borderline represents the threshold of acceptable cost elevation. (b–f) Three-way sensitivity analyses with regard to biopsy compliance (b), % complications of biopsy (c), cost of biopsy (d), cost of management of complication of biopsy (e) and prostate cancer prevalence (f) in addition to the specificity and cost differences. The inclination of borderline varies within the gray zone of each graph according to changes in the tested parameters indicated in each graph.

Table 3 Sensitivity analysis

	Base case	Range	Threshold of acceptable cost elevation ($/%specificity)
Biopsy compliance (%)	70	40–100	0.679–1.698
% Complications of biopsy	5	0–20	1.019–1.698
Cost of biopsy ($)	150	75–300	0.679–2.207
Cost of management for complication of biopsy ($)	500	200–2000	0.847–2.896
Prostate cancer prevalence	0.244	0.01–0.30	1.213–0.924†

†Inverse correlation with prostate cancer prevalence.

PSA was more expensive by $9.40 than that using total PSA. The findings indicate that a 0.6% improvement in the primary screening at the same price provides a $0.60 cost reduction per participant, which is almost identical to our results.

Three-way sensitivity analyses of the present study showed that biopsy compliance and the cost of biopsy have a larger impact on the threshold of acceptable cost elevation for the specificity improvement compared to the other tested items (Fig. 2). This seems partly because of a wide range within which the sensitivity analysis was run. However, practical biopsy compliance in the reported screening programs ranged from less than 25% to more than 90% (Table 1). Since the impact of the specificity on the total screening cost is greater where biopsy compliance and costs of biopsy are high, use of a more specific measure is strongly recommended even if it is costly to some degree.

There are some limitations of the present study. The basis of this kind of study on prostate cancer mass screening is that prostate cancer screening is beneficial for improvement in disease-specific mortality or quality-adjusted life length. If the screening were not beneficial, this study would be irrelevant. This issue is still controversial[4,5] and there has been no definitive result of a prospective randomized control study. However, since the present study is a cost analysis and does not deal cost-effectiveness, the study would be meaningful as far as prostate cancer detection is based on a primary test such as PSA, and a secondary diagnostic test such as biopsy.

There may be criticism that it is impractical to assume the sensitivity of two primary screening measures are identical. Certainly, identical sensitivities seem unlikely and even a small difference in the sensitivity can be a big difference in both the cost and the effect of prostate cancer screening. However, we simply studied the impact of specificity change on the total cost of screening. This model is rather suited to the control sensitivity of primary screening tests at any level. Indeed, PSA-associated markers have been compared based on the specificity for each cut-off providing equivalent sensitivity in a lot of previous reports.[6] In most reports, the cut-off value for the primary screening test is set at the same level as a sensitivity of 0.90–0.95, and the more specific marker in the high sensitivity range was considered valuable.

Since we studied the costs for a screening program only, as the outcome of the decision-analytic model, non-pecuniary factors such as improvement in the quality-of-life of participants, and the practical use of medical resources were not incorporated. Benefits from improvement in the specificity and consequent decrease in unnecessary biopsies include not only cost reduction but also improvement in quality-of-life, economy with time and saving of other medical resources. In this regard, Gyrd-Hansen and Sogaard investigated willingness-to-pay for a decrease in risk of a false positive result of a primary screening test using a breast cancer screening model.[20] They estimated the willingness-to-pay for a 1% reduction in risk of false positive diagnosis over a lifetime (10 screening tests) as 590–890 Danish krones (about US$95–143).

A plain comparison between screening programs for breast and prostate cancers should be interpreted with caution since there are substantial differences between screening programs for the two cancers in the accuracy of the primary screening tests and the burden of secondary screening, ceteris paribus. Nevertheless, results of the previous study seem to indicate that improvement in the quality-of-life by averting unnecessary secondary screening tests has a far greater magnitude of significance compared to direct cost reduction. If data that is specific to prostate cancer screening had been provided, we should have analysed the quality of life-related outcomes including willingness-to-pay as well as the screening cost. Unfortunately, there has been little data on quality-of-life utilities with regard to prostate cancer screening procedures. Improvement in the specificity should be at least high-rated additively with non-pecuniary advantages including improvement in the quality-of-life and the saving of medical resources, when the total societal health burden is considered in the comparison between the two different primary screening tests.

As another limitation of this study, it should be noted that only a linear regression type association between the cost and specificity of a primary screening test was considered. It is true from the viewpoint of screening promoters introducing a new primary screening test into an existing screening program since the impact of a 1% improvement in the specificity on the total screening cost is constant at any specificity level. However, it is quite an impracticable idea from the viewpoint of manufacturers of screening tests, since it is apparently more difficult and expensive to improve the specificity at higher levels, for instance, from 99% to 100% compared to 20% to 21%. If the price of a primary screening test reflects the developmental costs, the price increase rate will be higher in higher ranges of the specificity, and consequently, the isocost curve for the total screening costs will be expressed as a concave function. From a converse point of view, it can be recommended for the manufacturers to develop a new assay kit with higher specificity, as the price increase due to the developmental cost falls into the acceptable cost elevation. In this regard, this model is helpful not only for screening promoters but also for manufacturers of new markers for prostate cancer screening.

Conclusion

The specificity of primary screening tests has a significant impact on the total cost of prostate cancer mass screening. On the development and introduction of a new primary screening test, we should consider the acceptable cost elevation for the community to which the screening program is applied. The findings of this study could provide important evidence until a randomized control study incorporating quality-of-life and medical resources is performed to evaluate the real cost-effectiveness of prostate cancer screening programs using different primary screening tests.

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INTERNAL MEDICINE

□ LETTERS TO THE EDITOR □

Aspirin for Primary Prevention of Cardiovascular Disease in Japan

Takeshi Morimoto[1] and Kunihiko Matsui[2]

Key words: aspirin, coronary heart disease, primary prevention

(DOI: 10.2169/internalmedicine.46.0212)

To the Editor We read the economic evaluation article of aspirin for the primary prevention of cardiovascular disease in Japan by Tsutani et al with interest (1). They estimated the potential benefit and costs from a hypothetical simulation model based on published data and assumptions. They concluded that aspirin therapy should be recommended in the primary prevention of cardiovascular disease in all individuals who have at least a moderately increased risk of coronary heart disease and who do not have an increased risk of gastrointestinal bleeding events. Their conclusion was derived from an assumed 1.5% annual risk of coronary heart disease based on guidelines from other countries. We question whether such guidelines are valid in Japan. Who was at increased risk of gastrointestinal bleeding?

The absence of well-designed cohort studies, such as Framingham study to estimate the risk of cardiovascular disease and clinical trial of aspirin for primary prevention is an apparently critical issue in Japan (2, 3). We, however, analyzed the potential effects of aspirin as a primary prevention strategy against coronary heart disease in the same manner as the US Preventive Service Task Force (4, 5). We compiled published data on incidence of coronary heart disease, strokes, and gastrointestinal bleeding, and applied the risk ratios of aspirin from the US studies to the Japanese population. We concluded that aspirin should be considered for those with a 5-year coronary heart disease risk of 6 to 14% based on the individual risk factors. The 1.5% threshold of annual risk for coronary heart disease (5-year risk, 7.5%) indicated by Tsutani et al was consistent with our threshold for middle-aged men, but such thresholds should be carefully adjusted by other risk factors like the US guidelines and our analyses (4, 5).

We do not intend to imply that the analyses of Tsutani et al (1) are incorrect, but we argue the process from which their recommendation was derived and the target population should be explicitly clarified. Because the risks of cardiovascular disease in Japan are different from those in Western countries, the risk calculation methods used in such countries should not be applied (5). Although they conducted simple one-way sensitivity analyses and commented that they used data from other countries, their results are weak and their conclusion is likely to overemphasize implications to Japanese healthcare providers and patients. These issues in particular should be carefully scrutinized by authors and reviewers when the authors have a relationship with manufacturers of products which they deal with in the manuscript.

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INTERNAL MEDICINE

□ REVIEW ARTICLE □

Physical Diagnosis of Chronic Obstructive Pulmonary Disease

Yasuharu Tokuda[1] and Seishirou Miyagi[2]

Abstract

Among the various diagnostic strategies of chronic obstructive pulmonary disease (COPD), physical diagnosis is the quickest and requires no extra cost. Rapid physical diagnosis of COPD in primary care practice can lead to earlier actions of preventive measures and counseling for patients. Further, rapid physical diagnosis of COPD in an emergency department is also crucial for timely use of potentially lifesaving therapy specific for COPD patients. In this review, we will present a broad scope of physical findings for rapid physical diagnosis of COPD.

Key words: chronic obstructive pulmonary disease, physical examination, inspection, percussion, palpation, auscultation, vital sign, acute exacerbation

(DOI: 10.2169/internalmedicine.46.0455)

Introduction

Chronic obstructive pulmonary disease (COPD) is a major global health concern. However, undiagnosed chronic obstructive pulmonary disease is common in the general population and is associated with impaired health (1, 2). Among the various diagnostic strategies of COPD, physical diagnosis is quickest and less expensive, and this can lead to earlier actions of secondary prevention. Rapid physical diagnosis of COPD is important even in patients free of pulmonary symptoms, since this can lead to more intensive counseling on smoking cessation and vaccination against influenza and pneumococcal infections. Thus, in settings such as primary care practice, home-based, and community-based care, rapid physical diagnosis of COPD is also still useful and important.

Rapid physical diagnosis of COPD is crucial also in an emergency department for timely use of potentially lifesaving therapy with bronchodilators or systemic steroids in patients with acute exacerbation of COPD, whose previous clinical history (indicating the presence of COPD) may be unavailable at the time of arrival to an emergency department. Moreover, the clinical recognition of COPD by physical diagnosis may have time, cost, and convenience advantages compared to pulmonary function testing and computed tomography. Thus, in this review article, we will present a broad scope of physical findings of COPD (Table 1). In addition to physical findings for rapid diagnosis of COPD, we will also present interpretation of vital signs for assessing the severity of acute exacerbation of COPD.

Inspection

Pursed-lip breathing

Patients with COPD tend to exhale with pursed-lips. In this way, they increase expiratory airway resistance to elevate pressure inside the small collapsible airways for preventing alveolar collapse or slow the breathing frequency (3). Because the airways are not at risk of collapse during inspiration, many patients, who do purse their lips, do it unconsciously only during expiration. This is considered as a form of self-administered positive end-expiratory pressure (4).

Use of accessory muscles of respiration

This finding may be accompanied by increased activity of sternocleidomastoid and scalenus muscles in patients with COPD (5). With chronic compensatory use, sternocleidomastoid muscles may develop noticeable hypertrophy and they will be thicker than the patient's own thumb (6). On

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Table 1. Useful Physical Signs for Diagnosis of COPD

Inspection
Pursed-lip breathing
Use of accessory muscles of respiration
Jugular venous distension during expiration
Retraction of supraclavicular fossa during inspiration
Short trachea
Respiratory paradox (respiratory alternans)
Muscle wasting
Increased antero-posterior chest diameter (barrel chest or pulmonary kyphosis)
Loss of pump-handle and bucket-handle movements of the chest
Peripheral edema
Dyspnea-relieving posture
Hoover's sign
Palpation
Restricted chest expansion
Exaggerated bulging of the intercostal spaces
Subxiphoid shift of a point of maximum impulse of the heart
Percussion
Chest hyperresonance
Drop heart (microcardia)
Auscultation
Diminished lung sounds
Early inspiratory crackles
Amphoric Breathing (jar breathing; cavernous breathing)
Accentuated P2
Special maneuver
Forced Expiratory Time (FET)
Match test (Snider test)
Vital signs for assessing the severity of acute exacerbation
Pulsus paradoxus

COPD: chronic obstructive pulmonary disease.

the contrary, hypertrophy of scalenus muscles is more likely identified in patients with restrictive lung disease (6).

Jugular venous distension during expiration

An inspection of the neck veins usually involves an estimation of jugular venous pressure and an analysis of the venous pulse (7). However, jugular venous pressure may be difficult to assess in patients with severe lung hyperinflation because of marked respiratory variations in intrathoracic pressures (8). Jugular venous distension during expiration indicates an increased positive pressure in the thorax of patients with COPD (9). The presence of a prominent jugular V wave with loss of X decent (CV merger) may indicate cor pulmonale with tricuspid valvular regurgitation (10). Figure 1 presents jugular venous wave forms in patients with COPD with tricuspid regurgitation and in normal controls. Additionally, hepatojugular reflux is a useful adjunct to jugular venous distention in the diagnosis of cor pulmonale with tricuspid regurgitation (11).

Retraction of supraclavicular fossa during inspiration

Retraction of supraclavicular fossae during inspiration is due to excessive swings of intrathoracic pressure, and this finding probably results from a phase lag between the generation of negative pleural pressures and the resultant change in lung volume (12). One study found significant correlation between the reduced forced expiratory volume in one second (FEV1) and the presence of this finding (13).

Short trachea

The distance between the suprasternal notch and the lower edge of thyroid cartilage is 3 to 4 digits in width in normal individuals, while this may be shortened to about 1 to 2 digits in patients with COPD (12). The configuration of trachea is distorted in patients with COPD and the ratio of the short to the long radius of trachea is smaller in patients with COPD than in normal controls (14).

Respiratory paradox (respiratory alternans)

Normally, the abdominal wall moves passively outward during inspiration, as the descending diaphragm squeezes the intraabdominal contents down and outward. Then the abdominal wall retracts during expiration as the diaphragmatic piston returns to its resting position. By progressive weakness of the diaphragm due to overwork in severe COPD, the weak diaphragm is passively sucked upwards in inspiration as the intercostal muscles do the work of inspiration; the abdominal wall retracts during inspiration (15). This is called the respiratory paradox (16). Patients with this sign usually

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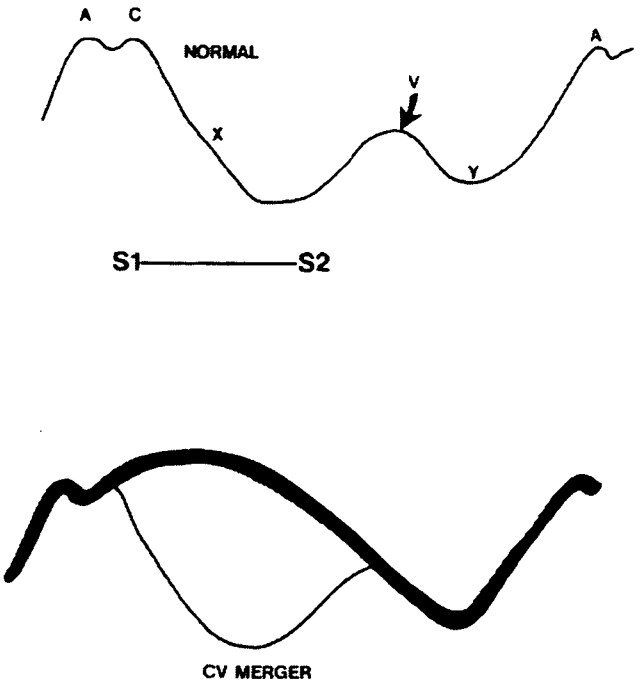

Figure 1. Jugular Venous Pulsations. Upper; normal wave form: Lower; tracing of patients with tricuspid regurgitation, superimposed on the normal wave form. A=atrial contraction; C=carotid transmission (not visible clinically); X=descent in right atrium following A; V=passive venous filling of atria from the venae cavae; Y=descent during atrial resting phase before contraction. CV merger indicates the merged wave of C and V waves. S1 and S2 denote the first and second heart sounds, respectively (27, 57). Arrow indicates v wave.

have severe ventilatory failure and may be in need of mechanical ventilation.

Muscle wasting

Patients with advanced COPD gradually lose weight and show muscle wasting that is attributed to immobility, hypoxia, or release of systemic inflammatory mediators, such as the tumor necrosis factor (17). Lower body mass index is included into a multidimensional grading system (BODE index) as a significant predictor of hospitalization for COPD (18, 19).

Increased antero-posterior chest diameter (barrel chest or pulmonary kyphosis)

Because patients with COPD undergo significant weight loss, the increased antero-posterior chest diameter may be an illusory finding from an image effect due to a decreased antero-posterior abdominal diameter (20).

Loss of pump-handle and bucket-handle movements of the chest

In the normal respiratory movement by inspection from the lateral side, one will see a pump handle-like movement of the chest with the point of the sternal angle (angle of Louis) as a fulcrum shaft. In addition, by inspection from the front, one will see a bucket handle-like outward movement of the bilateral contours of the rib cage during inspiration. With increased disease severity, patients with COPD may lose these movements, which indicate that %FEV is less than 40% (12, 21).

Peripheral edema

The presence of significant edema may indicate right-sided heart failure or cor pulmonale in patients with pulmonary hypertension from severe COPD. Edema can also be present if pCO_2 is elevated over 65 mmHg because of oliguria due to redistribution of renal blood flow from cortical to medullary areas of kidneys (22-25). Hypoxia less than 40 mmHg of PO_2 can also cause renal vasoconstriction and subsequent oliguria and edema (23). Patients with COPD and peripheral edema have a 5-year survival rate of only about 30% (26).

Dyspnea-relieving posture

It is important to observe what position the patient assumes for most comfortable breathing to improve respiratory mechanics (27). Patients with more advanced disease may have postures that relieve dyspnea, such as leaning forward against outstretched palms (27).

Hoover's sign

With the patient supine, the examiner should lightly rest the right hand on the patient's left hypochondrium, with the thumb on the medial costal margins and the remaining fingers superiorly toward the patient's head. Then the examiner should lightly place the left hand on the patient's right costal margin, symmetric to the right hand. The patient should be instructed to take a deep breath. Normally, both hands will swing out symmetrically during inspiration and the thumbs will form a more obtuse angle, returning to a more acute angle with expiration. The hands are not to offer resistance, but only to increase the appreciation of the change in angle. With practice, the examiner can observe this sign without using the hands (27). The change of this angle during inspiration is determined by the balance between two forces: the lateral pull on the costal margins due to the intercostal muscles and the contrary action of the diaphragm normally exerted only at end-expiration when the diaphragm is flat. When the diaphragm is sufficiently flattened in early inspiration, as in COPD, its muscle fibers pull horizontally rather than vertically and might overcome the action of the intercostal muscles, causing the costal margin to move medially during inspiration and causing the angle to become more acute (28, 29). This sign has also been called Hoover's groove, because one can sometimes see a groove as the flattened diaphragm pulls inward. Hoover's sign may be lost if the patient leans forward, because the increased abdominal pressure causes the diaphragm to take a more convex orientation (30).

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Palpation

Palpation of the chest is limited since the bony rib cage hides many abnormalities of the lungs. However, palpation of the chest in patients with COPD may detect abnormal respiratory excursion. Respiratory excursion can be assessed when the patient breathes in and out, either by simultaneous palpation of symmetric areas of the chest or by measurement of the changing circumference (31). In addition, palpation in patients with COPD should also include locating a point of maximum impulse of the heart. Tactile fremitus also seems to be decreased in patients with COPD.

Restricted chest expansion

Restricted expansion can be quantitated by measuring the difference in circumference of the chest between end-expiration and end-inspiration with a tape measure placed at the nipple line (32). The normal value has been stated to be 5 cm: An expansion of 3.8 cm or less is considered impaired (33). As a general rule, a single measurement of less than 2.5 cm is definitely abnormal, while a measurement of more than 7.6 cm is normal (27).

Exaggerated bulging of the intercostal spaces

Normally, the intercostal spaces bulge inward during inspiration and outward with expiration. An exaggeration of the inspiratory retraction occurs in patients with COPD. The mechanism of this finding is likely due to an imbalance between the ability of the respiratory muscles to create a negative intrapleural pressure and the impaired ability of the lungs to expand (27). Exaggerated expiratory bulging of the intercostal spaces also results from a mechanism similar to that of heightened inspiratory retraction (34). Diffuse expiratory bulging suggests that the lungs are not being emptied because of an increased expiratory airway resistance.

Subxiphoid shift of a point of maximum impulse of the heart

Patients with COPD may not have a point of maximum impulse of the heart (PMI) in the expected place (35, 36). This is also called an "absent" apical impulse. PMI may be found in the subxiphoid region, which suggests that %FEV1 is less than 50% (12). In addition, a systolic para-sternal heave may indicate the presence of right ventricular hypertrophy (7).

Percussion

Chest hyperresonance

The chest of patients with COPD should be percussed to determine the quality of the sound that resonates. If the sound is more hollow than normal, the chest is called hyperresonant (37). Generalized and symmetrical hyperresonance on percussion is a valuable finding suggestive of COPD.

Drop heart (microcardia)

On percussion, the heart of patients with advanced COPD may be noted in small and vertical shape (38). This finding is sometimes referred to as a drop heart (shaped like a teardrop) or as microcardia, which should suggest strongly the presence of subclinical emphysema (38).

Auscultation

The recommended terms for adventitious lung sounds, based on their acoustic characteristics, are crackles for discontinuous sounds and wheeze or rhonchus for continuous sounds (39). Wheezing will sound like high-pitched musical tones, while rhonchi will sound like lower-pitched wheezes (40). In auscultation, patients with COPD often present with diminished lung sounds, prolonged expiratory time, and expiratory wheezing that initially may occur only on forced and unforced expiration (27, 41). One may hear coarse crackles beginning with inspiration (early inspiratory crackles). Cardiac auscultatory signs of COPD include distant heart sounds, sometimes best heard in the epigastrium.

Diminished lung sounds

Although breath sound intensity is insensitive to mild degrees of ventilatory impairment (42), definitely reduced intensity is a strong indicator of obstructive pulmonary disease, and normal breath sounds virtually exclude the possibility of severe COPD (43, 44). Another study stated that diminished breath sounds are also the best predictor of moderate-to-severe COPD (36).

Early inspiratory crackles

Crackles in the early inspiratory phase correlate with obstructive lung disease involved with medium to large airways, while late inspiratory crackles are associated with interstitial lung disease (40, 45). Early inspiratory crackles occurring in patients with COPD generally mean that the % FEV1 is less than about 40% (45). Early inspiratory crackles can radiate through the mouth of COPD patients so that one can hear it by holding the stethoscope in front of the opened mouth (23). In contrast, crackles from congestive heart failure do not radiate through the opened mouth (7). Early-to-mid inspiratory crackles indicate the presence of bronchiectasis (46).

Amphoric breathing (jar breathing; cavernous breathing)

Amphoric breathing resembles tracheal breathing in that the two phases (inspiratory and expiratory) are much closer to each other in amplitude and duration than in normal vesicular sounds. However, amphoric breathing has a more resonant and harmonious timbre than tracheal breathing, and it is heard where vesicular breath sounds are expected (27). Amphoric breathing indicates a cyst, bleb, bulla, or other air-containing space in the lung, which is in communication

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with the bronchial system. Cavities with rigid and inflexible walls can produce the best amphoric breath sounds, whereas a resilient and deformable cavity would produce no amphoric sounds due to the lack of vibrations (27). Once a cavity appears and produces amphoric breathing, it should be permanent. Thus, disappearance of a previously noted area of amphoric breathing may suggest that something has filled the cavity, such as blood, pus, or aspergilloma (27).

Accentuated P2

Signs of cor pulmonale in COPD include splitting of the 2nd heart sound with an accentuated pulmonic component, which is an indication of pulmonary hypertension (7). Further, tricuspid regurgitation murmur may indicate the presence of right ventricular dilatation. This murmur can be differentiated from left side murmur by noting an increased intensity of the tricuspid regurgitation murmur during inspiration, described as Carvallo's sign (11).

Special Maneuver

Forced expiratory time (FET)

The bell of a stethoscope should be placed over the trachea in the suprasternal notch and a stopwatch should be set to zero. The patient should be instructed to take in the deepest breath possible and then to blow it all out as fast as possible. As the patient begins to exhale, the stopwatch should be started. As soon as audible expiration is no longer heard, the stopwatch should be turned off. An FET of more than 6 seconds indicates considerable expiratory airflow obstruction with %FEV1 <50% (47). Three trials with averaging the results are usually recommended. This clinically measured forced expiratory time correlates well with the forced expiratory time measured by spirometry, the latter being almost one second greater on the average (47) .

Match test (Snider test)

The patient is asked to huff a match out. Huffing is performed with the mouth and lips as wide open as possible. The normal individual can huff a match out at 15 to 20 cm on the first try (27). Patients with moderate-to-severe COPD have great difficulty with this test (48). Some require multiple trials to huff out the match at 15 cm, and some with severe disease are unable to accomplish this. Using a cutoff of 10 cm is a good test to rule in moderate severity of COPD (36). Use of therapeutic oxygen in patients with COPD is a contraindication to this test.

Vital Signs for Assessing the Severity of Acute Exacerbation of COPD

Blood pressure

Hypercapnia may cause transient hypertension with wide pulse pressure, sometimes along with hot hands (5 mmHg or a higher increase from the baseline value in PCO2), flapping tremor (15 mmHg or a higher increase from the baseline value in PCO_2), and cold sweat (49-51). Symptomatic hypotension with oliguria can also be induced by an extremely severe hypoxia (PO_2 <20 mmHg).

Heart rate

Both hypoxia and hypercapnia can induce tachycardia by an increased release of catecholamine (49). Severe hypoxia or hypercapnia can cause arrhythmia such as multi-atrial tachycardia, atrial fibrillation or ventricular tachycardia (52, 53).

Respiratory rate

The respiratory rate increases proportionally to disease severity. Rapid and shallow respirations of more than 40 per minute may cause respiratory muscle fatigue, and this finding along with respiratory acidosis suggests indication for mechanically assisted ventilation (49, 54). A respiratory rate of less than 7 per a minute with hypercapnia indicates an impending respiratory arrest (49).

Body temperature

Temperatures over 38.5 or under 35.5 Celsius require careful attention, particularly considering the possibility of sepsis. Shaking chills, or moderate chills along with tachycardia or tachypnea, are a hallmark of sepsis (55).

Pulsus paradoxus

While measuring blood pressure, one can determine whether there is pulsus paradoxus. During tidal breathing, the cuff is inflated to above the systolic blood pressure. The cuff pressure is slowly released until the first Korotkoff sound is heard only during expiration; this value of systolic blood pressure is then noted. The cuff pressure is further reduced until the first Korotkoff sound is heard throughout inspiration; this value of systolic blood pressure at this point is also noted. The systolic blood pressure is normally lower during inspiration than during expiration. If the difference between these two pressures is at least 15 mmHg, the patient has pulsus paradoxus, and %FEV1 is likely to be 25% or lower (23, 37). Moreover, this difference is more accentuated, as the patient has a more severe degree of acute exacerbation (56).

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