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Efficacy of Computed Tomography (CT) Attenuation Values and CT Findings in the Differentiation of Pleural Effusion

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Summary

Background: The aim of this study was to investigate the efficacy of computed tomography (CT) findings for characterizing pleural effusions with the use of attenuation values.

Material/Methods: One hundred and twenty eight patients with pleural effusions on thoracic CT who underwent thoracentesisis within two weeks were studied. Pleural effusions were classified as exudates or transudates according to the Light's criteria. A region of interest was placed for the measurement of Hounsfield Unit (HU) values in the area of the greatest amount of effusion on each slice of the three slices used. CT features that were evaluated for distinguishing pleural exudates from transudates included pleural nodules, pleural thickening and loculation.

Results: Thirty three (26%) of the 128 pleural effusions were transudates and 95 (74%) were exudates. The mean HU values of the exudates (8.82±7.04) were significantly higher than those of the transudates (2.91±8.53), ($p<0.001$). No statistically significant difference was found between transudate and exudate patients in terms of pleural thickness, pleural nodules and loculation ($p>0.05$).

Conclusions: HU values can help in differentiating exudative pleural effusions from transudative pleural effusions. Because of overlapping HU values, correlation with clinical findings is essential.

MeSH Keywords: Exudates and Transudates • Multidetector Computed Tomography • Pleural Effusion

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Background

Pleural effusion is defined as an abnormal fluid collection in the pleural cavity [1]. In healthy people, this cavity contains a small amount of fluid secreted by parietal pleura (0.25 ml/kg) [2]. The balance between the processes of secretion and absorption can be disturbed in certain clinical conditions, which results in abnormal fluid accumulation in the pleural cavity [1]. Pleural effusions are divided into transudative and exudative [3]. Differentiation between a transudate and an exudate is important for clinical management. In transudative effusions, capillary beds of pleural membranes are intact, and fluid accumulates in the pleural space due to either increased hydrostatic pressure or decreased oncotic pressure [4]. Congestive heart failure(CHF), cirrhosis and nephritic syndrome are the most common causes of transudative effusions [5]. In exudative effusions, the capillary beds themselves are affected by disease. Abnormal fluid accumulation in the pleural space d results from an increased permeability of the capillary beds [6]. The most common causes of exudative effusions include inflammation, infection and malignancy [7].

Although medical history, physical examination and imaging studies may give important clues as to the cause of pleural effusions, all cases should be evaluated with thoracentesis to obtain a final diagnosis [8]. For the past several decades, transudates have been differentiated from exudates according to the Light's criteria that require measurements of the levels of protein in the pleural fluid and

serum [9]. Thoracentesis is an invasive diagnostic method which is associated with iatrogenic complications [10]. Pneumothorax, hemothorax, reexpansion pulmonary edema and organ laceration are the major complications of thoracentesis [11]. The most common minor complications include pain, cough, shortness of breath, and hematoma [12]. There are no absolute contraindications to thoracentesis. Relative contraindications to thoracentesis include coagulopathy and other bleeding disorders [13]. Computed tomography(CT) can be used to distinguish transudates from exudates to avoid these complications [14]. There are only few studies that have investigated the relationship between CT features, such as pleural nodules, pleural thickening, loculation and effusion density, and different types of pleural effusion(transudate or exudate). However, these reports have conflicting and sometimes contradictory results [14–17].

The aim of this study was to investigate the efficacy of CT findings in characterizing pleural effusions using attenuation values.

Material and Methods

One hundred and twenty eight (51 men, 77 women; mean age 59.93±14.65 years; range, 15–87 years) patients with pleural effusions on thoracic CT who underwent diagnostic thoracentesisis within two weeks, from 2012 to 2014, were retrospectively studied. The study protocol was approved by the Ethics Committee of our hospital. The laboratory findings of pleural effusions (protein, albumin, glucose, and lactate dehydrogenase (LDH) levels) as well as the data on the causes of pleural effusions were determined from the medical records of the patients. Pleural effusions were classified as exudates or transudates according to the Light's criteria [9]. These criteria classify effusions as exudative if one or more of the following findings are present: (a) the ratio of pleural fluid total protein to serum total protein is greater than 0.5, (b) the ratio of pleural fluid LDH to serum LDH is greater than 0.6, or (c) pleural fluid LDH level is greater than two thirds of the upper limit of the normal serum LDH level [9]. Patients were excluded from the study if they had pleural tubes prior to CT imaging, unacceptable image quality and unclear causes of pleural effusion.

All CT examinations were performed with a Somatom Sensation 40-MDCT scanner (Siemens Medical Solutions, 2010). All CT scans were obtained with the following parameters: 120 kV peak, automated mA, slice thickness of 1–10 mm, 1 pitch. Scans were obtained from the level of the thoracic inlet to the caudal edge of the kidney. Contrast-enhanced CT was performed in 73 patients. All of these patients underwent standard chest CT examination after a standard injection protocol(100 mL, iopamidol 300). Injection rate was 2.5 mL/s. Intravenous(IV) contrast material was not administered to patients with renal dysfunction or known allergy to contrast material, or when there was no indication for the use of contrast material for diagnosis. All CT scans were evaluated independently by two experienced radiologists who were blinded to the clinical and laboratory findings. A region of interest(ROI) was placed for the measurement of Hounsfield Unit(HU) values in the area of the greatest amount of effusion on each slice of the three slices used (Figure 1). The greatest amount of effusion was determined by the largest anteroposterior diameter of the effusion. HU values were measured three times for each patient. The average of the three HU values was calculated. CT features that were evaluated for distinguishing pleural exudates from transudates included pleural nodules, pleural thickening(visible pleural line) and loculation(effusion which showed septations, was compartmentalized or accumulated in a fissure or a non-dependent portion of the pleura or showed a convex shape facing the lung parenchyma). For each patient, the mean CT attenuation values, the presence of pleural nodules, pleural thickening and loculation were recorded.

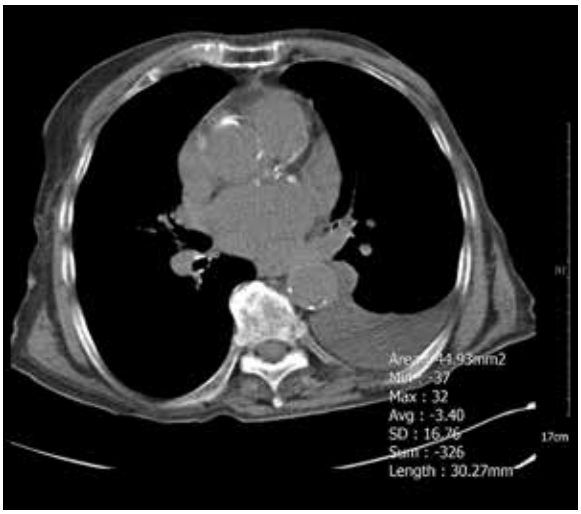

Figure 1. A region of interest(ROI) was placed for measurement of Hounsfield Unit(HU) values of the greatest amount of effusion on each slice of three slices used..

Number Cruncher Statistical System(NCSS) 2007 (Kaysville, Utah, USA) software was used for statistical analysis. Descriptive statistics such as mean, standard deviation, median, minimum, maximum, frequency and ratio values were reported in the tables. Independent samples t-test and the Mann-Whitney U-test were used to compare the variables between two groups. Qualitative variables were compared with Pearson chi-square test and Fisher's exact test. ROC curve analysis, sensitivity, specificity, PPV, NPV and accuracy values were used to determine cut-off values. Significance was set at $p<0.05$.

Results

According to the Light's criteria, 33(26%) of the 128 pleural effusions were transudates and 95(74%) were exudates, respectively. Demographic data and CT findings of the patients are shown in Table 1. Intravenous contrast material was used in 56 patients with exudative effusions and in 17 patients with transudative effusions, respectively. In patients with exudative effusions, the mean HU value was 8,38 (±6.20) for those who received IV contrast and 9.46 (±8.15) for those who did not receive IV contrast, respectively. In patients with transudative effusions, the mean HU value was 2,29 (±7.91) for those who received IV contrast and 3,56 (±9.36) for those who did not receive IV contrast, respectively. The injection of IV

Table 1. Demographic and CT findings of the patients.

		Min–Max	Mean ±SD
Age (years)		15 to 87	59.93±14.65
Effusion thickness (mm)		8 to 207	52.12
CT attenuation (HU)		–24 to 44	7.30±7.86
		N	%
Gender	Female	51	40
	Male	77	60
Pleural thickening		35	27
Pleural nodules		13	10
Loculation		30	23
Empyema		7	6
Malignancy		66	52
Parenchymal nodules		28	22
CHF		19	15
Pneumonia		22	17
Other causes of transudates		13	10
Other causes of exudates		1	1
Effusion	Transudates	33	26
	Exudates	95	74

Other causes of transudates include cirrhosis, Nephrotic syndrome and unknown. Other causes of exudates include tuberculosis.
HU – hounsfield unit; CHF – congestive heart failure.

Table 2. CT findings of the patients with exudative and transudative effusions.

	Patients with transudates (n=33)	Patients with exudates (n=95)	P
CT attenuation (HU)	2.91±8.53	8.82±7.04	[a]<0.001**
Pleural thickening	6 (18%)	29 (31%)	[b]0.170
Pleural nodules	1 (3%)	12 (13%)	[c]0.181
Loculation	8 (24%)	22 (23%)	[b]0.899

[a] Independent samples t test; [b] Pearsonchi-square test; [c] Fisher'sexact test. HU – hounsfield unit. Data are given as n (%) or Mean ±SD. ** p<0.01.

contrast did not significantly affect the HU values of transudative and exudative effusions (p>0.05). In patients who received IV contrast injections, the mean HU values of the exudates (8.82±7.04) were significantly higher than those of the transudates (2.91±8.53),(p<0.001). In patients who did not receive IV contrast, the mean HU value of the exudates (9.46±8.15) was significantly higher than that of the transudates (3.56±9.36), (p<0.001). No statistically significant difference was found between transudate and exudate patients in terms of pleural thickness, pleural nodules and loculation(p>0.05). CT findings of the patients with exudative and transudative effusions are shown in Table 2. Based on the significant difference between transudate and exudate patients, ROC analysis and diagnostic tests were used for the determination of the cut-off point for the HU values. In cases with HU values above 5, sensitivity was found to be 72%, specificity 70%, positive estimation value 87% and negative estimation 46% for exudate detection, respectively. The area below the obtained ROC curve was 74% with the standard error of 5.4% (Figure 2). In terms of HU values, no statistically significant difference was found between patients with and without empyema (p>0.05). Moreover, as regards pleural thickness and the existence of pleural nodules, no statistically significant difference was found between patients with and without empyema (p>0.05). It was found that the frequency of loculation in patients with empyema (n=4, 57%) was higher than that in patients without empyema (n=26, 22%), although this was

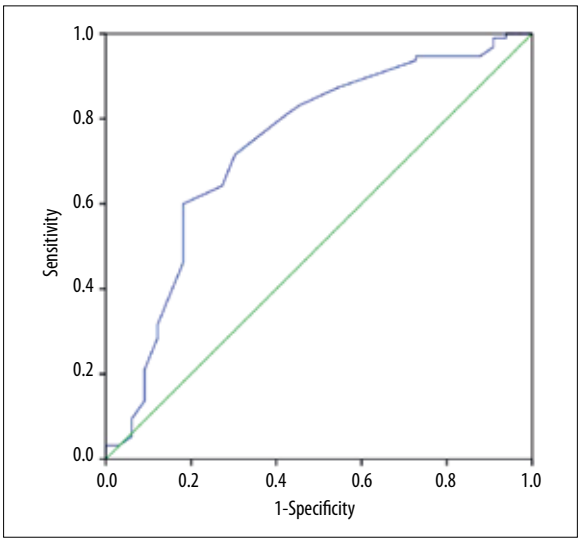

Figure 2. For the cases where the HU value is above 5, the area below the obtained ROC curve is 74% with a standard error of 5.4%.

not statistically significant (p=0.052). It was found that the HU values in patients with malignancies were significantly higher than those in patients without malignancies (p=0.012). No statistically significant difference was found between patients with and without malignancies in terms of the existence of pleural thickening and pleural nodules (p>0.05). It was found that the frequency of loculation in patients with malignancies (n=11, 17%) was considerably lower than that in patients without malignancies (n=19, 31%), although this difference was not statistically significant (p: 0.062). CT findings of the patients with and without malignancies are shown in Table 3. Based on the significant difference in the HU values between patients with and without malignancies, ROC analysis and diagnostic tests were used for the determination of the cut-off point for the HU values. In cases with HU values above 7, sensitivity was found to be 59%, specificity 61%, positive estimation value 62% and negative estimation 60% for malignancy detection, respectively. It was found that the HU values in patients with CHF were lower than those in patients without CHF at a statistically significant level (p=0.003). No statistically significant difference was found between patients with and without CHF in terms of the existence of pleural thickening and pleural nodules (p>0.05). It was found that the frequency of loculation in patients with CHF (n=8, 42%) was considerably higher than that in patients without CHF (n=22, 20%), although this difference was not statistically significant. CT findings of the patients with and without CHF are shown in Table 4. Based on the significant difference in the HU values between patients with and without CHF, ROC analysis and diagnostic tests were used for the determination of the cut-off point for the HU values. In cases with HU values above 5, sensitivity was found to be 79%, specificity 68%, positive estimation value 30% and negative estimation 95% for CHF detection, respectively. No statistically significant difference was found between patients with and without pneumonia in terms of HU values (p>0.05). No statistically significant difference was found between patients with and without pneumonia in terms of the existence of pleural thickening, pleural nodules and loculation (p>0.05).

Discussion

The pleural cavity, located between the parietal pleura covering the chest wall and the visceral pleura covering the

Table 3. CT findings of the patients with and without malignancy.

	Patients without malignancy (n=62)	Patients with malignancy (n=66)	P
CT attenuation (HU)	5.52±8.50	8.97±6.86	[a]0.012*
Pleural thickening	14 (23%)	21 (32%)	[b]0.241
Pleural nodules	4 (7%)	9 (14%)	[b]0.179
Loculation	19 (31%)	11 (17%)	[b]0.062

[a] Independent samples t test; [b] Pearson chi-square test. HU – hounsfield unit. Data are given as n (%) or Mean ±SD. * p<0.05.

Table 4. CT findings of the patients with and without CHF.

	Patients without CHF (n=109)	Patients with CHF (n=19)	P
CT attenuation (HU)	8.15±7.54	2.42±8.08	[a]0.003**
Pleural thickening	32 (29%)	3 (16%)	[b]0.221
Pleural nodules	13 (12%)	0 (0%)	[c]0.214
Loculation	22 (20%)	8 (42%)	[c]0.074

[a] Independent samples t test; [b] Pearson chi-square test; [c] Fisher's exact test. HU – hounsfield unit; CHF – congestive heart failure. Data are given as n (%) or Mean ±SD. ** p<0.01.

lung, contains a few milliliters of fluid in a healthy person. This fluid acts as a lubricant between the parietal and visceral pleura. Pathological accumulation of fluid in this cavity is defined as pleural effusion [18]. Pleural effusion should always be investigated using thoracentesis except when the effusion is clearly secondary to a specific underlying reason [19]. However, thoracentesis is an invasive method that is commonly associated with iatrogenic complications, particularly pneumothorax [10]. A noninvasive method to characterize pleural effusions could help avoid these potential complications. CT is helpful in distinguishing anatomic compartments of the thorax (e.g., the pleural cavity from lung parenchyma). This imaging method is useful also in distinguishing empyemas from lung abscesses, in detecting pleural masses and in determining loculated fluid collections [20]. Few published studies have evaluated pleural nodules, pleural thickening, loculation and density of effusion in patients with pleural effusions(14,15,16,17). These studies found different attenuation values for the evaluation of effusions.

Nandalur et al. [15] found that the mean attenuation values of exudates(17.1±4.4 HU) were significantly higher than those of transudates(12.5±6.3 HU; p=0.001). The authors determined that the mean attenuation values were moderately helpful in differentiating transudates from exudates. Abramowitz et al. [16] found that the mean attenuation values of exudates(7.2±9.4 HU) were lower than those of transudates(10.1±6.9 HU; p=0.24). Despite the lower mean attenuation values of exudates, the difference was not statistically significant. The use of attenuation values for characterizing pleural effusions was not recommended by both studies because of the overlapping attenuation values. In addition, both studies found that IV contrast did not affect the HU values. Therefore, they calculated the mean attenuation values of exudates and transudates regardless of the use of contrast agents [15,16]. However, Çullu et al. [17] found that in patients who received IV contrast, the mean attenuation values of exudates(14.5 HU) were significiantly higher than those of transudates(6.2 HU; p=0.001). They said that in patients who did not receive IV contrast, the mean attenuation values of exudates(13 HU) were significantly higher than those of transudates(6.1 HU; p=0.001). The authors determined that IV contrast did not significantly affect the HU values. They concluded that the mean attenuation values were useful for differentiating transudates from exudates. In our study, we found that the mean attenuation values of exudates(8.82 HU) were significantly higher than those of transudates(2.91 HU; p<0.001). When the cut-off value for exudative effusions were accepted as ≥5 HU, the sensitivity and specificity were 72% and 70%, respectively. Although the mean attenuation values of exudates were significantly higher than those of transudates, the sensitivity and specificity of the mean attenuation values for characterizing pleural effusions were found to be moderate. Therefore, it is essential that HU values be interpreted together with clinical findings of patients to fully characterize pleural effusions. Çullu et al. [17] reported that IV contrast agent was used in 50% of patients with transudative effusions and in 56% of patients with exudative effusions in their study. They found that the IV contrast agent did not affect the HU values. In our study, similarly to Çullu et al. [17], we found that IV contrast injection did not significantly affect the HU values of tansudative and exudative effusions(p>0.05).

Nandalur et al. [15] reported that CHF and empyema were predictors of the median HU values of pleural effusions, with a high and moderate sensitivity and specificity [15]. We found that CHF could be predicted with the use of the mean attenuation values of the effusions. When the cut-off value for CHF was accepted as ≤5 HU, the sensitivity and specificity were 79% and 68%, respectively. In contrast to Nandalur et al. [15], we did not find a concordance between attenuation values of pleural effusions and empyema. However, we found that malignant effusions were predictable using the mean attenuation values of the pleural effusions. When the cut-off value for malignant effusions was accepted as ≥7 HU, the sensitivity and specificity were 59% and 61%, respectively.

Arenas-Jimenez et al. [14] reported that the presence of pleural thickening, pleural nodules and loculation were highly specific for exudates. Pleural thickening was found in 75 patients, loculation in 24 patients and pleural nodules in 17 patients, all of which were exudates. Similar findings were found in the study by Aquino et al. [21] and Waite et al. [22]. T These authors reported that the presence of pleural thickening was highly specific for exudates. Çullu et al. [17] reported that, compared to transudates, exudates had a significantly higher frequency of loculation and pleural thickening. However, Abramowitz et al. [16] found pleural thickening in 8 out of 22 transudates (36%) compared to 46 out of 78 exudates (59%), and loculated pleural effusion in 8 of the 22 transudates (36%) compared with 45 of the 78 exudates (58%). Both pleural thickening and loculation were found in more than one-third of patients with transudates, which is not in line previous studies. In our study, similarly to Abramowitz et al. [16], we found that the presence of pleural thickening, pleural nodules and loculation were not reliable findings for characterizing pleural effusions.

Arenas-Jimenez et al. [14] reported that CT findings, such as loculation and pleural thickening, appeared more frequently in empyemas but also occured in pneumonic effusions; therefore, these findings cannot be used as a distinguishing feature. However, Çullu et al. [17] found that patients with empyemas had a significantly higher frequency of loculation and pleural thickening than other patients. In our study, there was no statistically significant difference in the frequency of pleural nodules and pleural thickening between empyema patients and other patients. However, it was found that the frequency of loculation in patients with empyemawas higher than that seen in patients without empyema, although this difference was not statistically significant (p=0.052). Arenas-Jimenez et al. [14] found that the presence of pleural nodules or nodular pleural thickening were the most sensitive and specific findings for the diagnosis of malignant pleural effusions. They concluded that when pleural nodules or nodular pleural thickening are seen on CT, the first diagnosis to be considered is a malignant effusion. In our study, there was no statistically significant difference in the frequency of pleural nodules and pleural thickening between malignant pleural effusions and other effusions. However, it was found

that the frequency of loculation in patients with malignancies was considerably lower than that in patients without malignancies, although this difference was not statistically significant(p=0.062).

Conclusions

We conclude that HU values can play a role in differentiating exudative pleural effusions from transudative pleural effusions. According to our study, exudative effusions can be considered when HU values are greater than 5. Then, sensitivity is 72%, specificity 70%, positive estimation value 87% and negative estimation 46%, respectively. On the other hand, because of overlapping HU values and the negative estimation value of nearly 50%, correlation with clinical findings is essential. In the literature, there are a few studies that have investigated the relationship between effusion density and the types of pleural effusion. However, cut-off HU values obtained in those studies are different [15–17]. Our results showed that additional CT parameters such as loculation, pleural thickness and the presence of pleural nodules are not reliable parameters for the differentiation of plural effusions. In conclusion, we believe that larger CT studies are needed to confirm our findings, and population and protocol based cut-off HU values must be determined. Population and protocol based cut-off HU values could help decrease the frequency of iatrogenic complications by reducing the need for thoracentesis.

Financial disclosure

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Conflicts of interest

There is no conflict of interest.

References:

1. Chung J, Perrot MD: Pleural effusion and empyema thoracis. In: Bope ET, Rakel RE, Kellerman RD (eds.), Conn's Current Therapy 2010. 1st ed. Philadelphia: Saunders/Elsevier; 2010; 263–65
2. Beers SL, Abramo TJ: Pleural effusions. Pediatr Emerg Care, 2007; 23: 330–34
3. Light RW: Diagnostic principles in pleural disease. Eur Respir J, 1997; 10: 476–81
4. Sahn SA: State of the art. The pleura. Am Rev Respir Dis, 1988; 138: 184–234
5. Kinasewitz GT: Transudative effusions. Eur Respir J, 1997; 10: 714–18
6. Miller E J, Idell S: Interleukin-8: An important neutrophil chemotaxin in some cases of exudative pleural effusions. Exp Lung Res, 1993; 19: 589–601
7. Longo DL, Fauci AS, Kasper DL et al: Disorders of the pleura and mediastinum. Harrison's Principles of Internal Medicine. 18th ed., 2011; Volume 1: 263
8. Light RW: Clinical practice. Pleural effusion. N Engl J Med, 2002; 346: 1971–77
9. Light RW, Macgregor MI, Luchsinger PC, Ball WC Jr.: Pleural effusions: The diagnostic separation of transudates and exudates. Ann Intern Med, 1972; 77: 507–13
10. Daniels CE, Ryu JH: Improving the safety of thoracentesis. Curr Opin Pulm Med, 2011; 17: 232–36
11. Thomsen TW, DeLaPena J, Setnik GS: Videos in clinical medicine. Thoracentesis. N Engl J Med, 2006; 355: 16
12. Sokolowski JW Jr., Burgher LW, Jones FL Jr. et al: Guidelines for thoracentesis and needle biopsy of the pleura. Am Rev Respir Dis, 1989; 140: 257–58
13. McVay PA, Toy PT: Lack of increased bleeding after paracentesis and thoracentesis in patients with mild coagulation abnormalities. Transfusion, 1991; 31: 164–71
14. Arenas-Jiménez J, Alonso-Charterina S, Sánchez-Payá J et al: Evaluation of CT findings for diagnosis of pleural effusions. Eur Radiol, 2000; 10: 681–90
15. Nandalur KR, Hardie AH, Bollampally SR et al: Accuracy of computed tomography attenuation values in the characterization of pleural fluid: An ROC study. Acad Radiol, 2005; 12: 987–91
16. Abramowitz Y, Simanovsky N, Goldstein MS et al: Pleural effusion: Characterization with CT attenuation values and CT appearance. Am J Roentgenol, 2009; 192: 618–23
17. Çullu N, Kalemci S, Karakaş Ö et alL Efficacy of CT in diagnosis of transudates and exudates in patients with pleural effusion. Diagn Interv Radiol, 2014; 20: 116–20
18. Light RW, Lee YCG (eds.), Textbook of pleural diseases. London: Arnold, 2003
19. Villena V, López Encuentra E, García-Luján R et al: Clinical implications of appearance of pleural fluid at thoracentesis. Chest, 2004; 125: 156–59
20. Mehta AC, Dweik RA: Pleural diseases. In: Stoller JK, Michota FA, Mandell BF (eds.): Cleveland Clinic Intensive Review of Internal Medicine. 4th ed. Philadelphia: Lippincott Williams & Wilkins, 2005; 452–66