Non-Specific Pleuritis after Medical Thoracoscopy: A Prospective Study

Pleurite Não Específica após Toracoscopia Médica: Um Estudo Prospetivo

Keywords: Pleural Effusion; Pleurisy/etiology; Thoracoscopy
Palavras-chave: Derrame Pleural; Pleurisia/etiologia; Toracoscopia

More than 50 causes of pleural effusion are known and, although the majority are benign (85%), both malignant and unknown causes are common.[1,2]

If the cause of pleural effusion is not found after thoracocentesis, a pleural biopsy is indicated. Medical thoracoscopy (MT) is considered the gold-standard for the diagnostic investigation of a pleural effusion with the highest diagnostic yield. Nevertheless, there are some clinical situations where the diagnostic accuracy of a 'blind biopsy' is high, like tuberculosis.[3-5]

Non-specific-pleuritis (NSP) is an inflammatory pleuritis that cannot be attributed to a specific cause. Malignancy is reportedly found in about 5% to 25% of cases (mostly mesotheliomas).[2]

We carried out a prospective study which followed patients with NSP after medical thoracoscopy and the aim was to assess the incidence rate of pleural malignancy.

Prior to the MT, all patients had a detailed medical evaluation, radiological assessment, and pleural fluid analysis via percutaneous lung biopsy. With some occasional exceptions, only patients with lymphocytic exudative pleural effusions without a known cause were referred to the MT procedure. The pleural fluid was classified as transudative or exudative according to the Light´s criteria exudative if pleural total protein/serum total protein ratio > 0.5; pleural lactate dehydrogenase/serum lactate dehydrogenase ratio > 0.6 or pleural effusion lactate dehydrogenase level greater than two-thirds the upper limit of the laboratory's reference range of serum lactate dehydrogenase.)

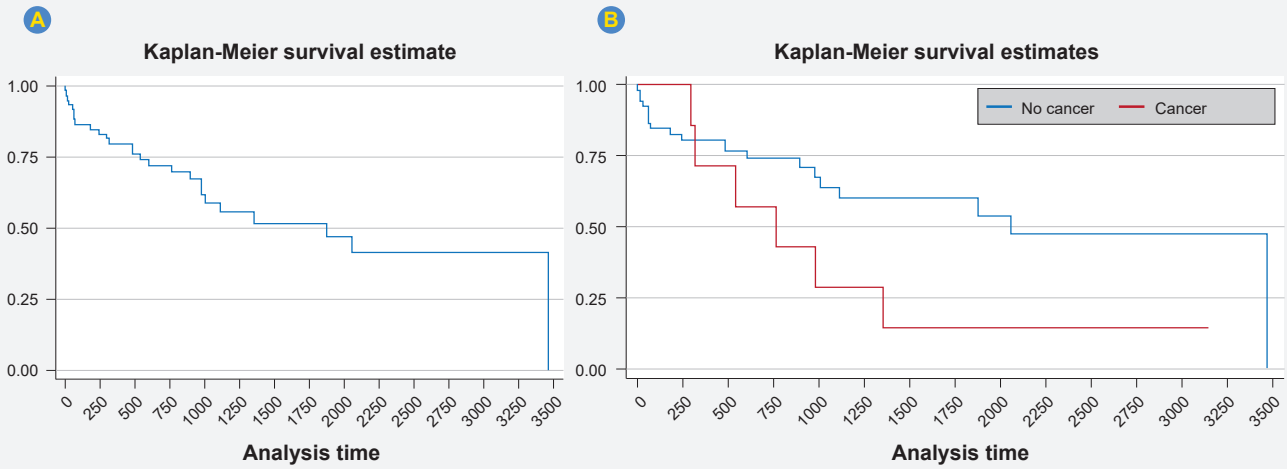
The data were properly anonymised and the study was carried out according to the principles of the declaration of Helsinki.

This study included the information extracted from electronic health records of patients that underwent medical thoracoscopy between 2011 and 2021 at a district hospital in Portugal. The patients were followed by a chest physician (appointments every three to six months after the diagnosis of NSP after MT) with regular chest X-rays or chest computed tomography to evaluate the relapse of the pleural effusion.

The end of follow-up was December 31, 2021 and patients were supervised until this deadline or until their death.

Data was analyzed using Stata® software, version 13 (StataCorp® LLC). Categorical variables are expressed as frequencies and percentages and continuous variables as means, standard deviations (SD), medians (Mdn/ Q2), quartiles (Q1, Q3), Skewness, and Kurtosis according to their distributions. Descriptive statistical methods were used for data analysis.

We plotted the Kaplan-Meier estimates (Fig. 1). The Kaplan-Meier estimator is a nonparametric estimate of the



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_t	Hazard ratio	Robust std. err.	Z	p > |z|	95% CI	
Malignancy	2.15	0.96	1.70	0.08	0.89	5.19
Age	1.03	0.01	2.02	0.04	1.00	1.06
Sex	1.18	0.45	0.44	0.66	0.55	2.52

Figure 1 – Survival analysis. (A) Kaplan-Meier survival-curve; (B) Kaplan-Meier survival-curve of patients with cancer and without cancer; (C) Hazard-ratios.

probability of survival past a given time or, of the probability of failing after that given time. We also used a Cox proportional hazards model, which is a semiparametric model, and which extended the survival analysis methods to assess the effect of several risk factors on survival time simultaneously.

During the 10-year-follow-up, a total of 238 MT were performed. The mean age was 69.0 years (SD ± 15.04) and most patients were male (54.6%).

The predominant diagnosis was pleural malignancy (47.9%), followed by NSP (24.8%).

Regarding the 59 cases of NSP, mean-age was 70.0 years (SD ± 14.41) with 64.4% males. This subset of patients had an average follow-up of 1003 days (SD ± 836.82; Q_1 = 465; Q_2 = 799; Q_3 = 1354; Skewness = 1.12; Kurtosis = 3.62).

During follow-up, 11.9% (n = 7) of patients with NSP (n = 59) received a diagnosis of malignant pleural effusion, while the cause of the pleural effusion in the other patients was non-malignant.

The average time-to-diagnosis was 773 days (SD ± 1037.06; Q_1 = 73; Q_2 = 323; Q_3 = 942; Skewness = 1.62; Kurtosis = 4.22). Diagnostic confirmation of two patients was achieved after video-assisted thoracoscopic surgery (VATS) and five patients with thoracocentesis. Histologically, most cancers were lung cancer (n = 2), gastrointestinal (n = 2), mesothelioma (n = 1), ovarian cancer (n = 1) and urothelial cancer (n = 1). At the end of the follow-up period, only one patient was still alive. Most patients were nonsmokers (71.4%).

The average time until death in patients initially with NSP that subsequently presented malignant pleural-effusion was 309 days (SD ± 197.79; Q_1 = 204; Q_2 = 267.50; Q_3 = 441; Skewness = 0.28; Kurtosis = 2.21).

Regarding survival analysis of patients with NSP, the Kaplan-Meier survival-curve in Fig. 1A showed that that the survival estimates rapidly declined until the 100th day. Then, it continued to decline at a slower pace until it reached 75% around the 500-day mark. After that, the chance of survival rapidly decreased until the 2000-day mark (below 50%).

In Fig. 1B, the estimate of survival was lower for patients with cancer and the difference between the probabilities became larger with time.

Regarding hazard-ratios in Fig. 1C, age was associated with an increased risk of death (p = 0.04). Each year of age increased the risk of death by 3% [HR = 1.03, 95% CI = (1.00; 1.07)] Moreover, malignant pleural effusion during follow-up was associated with an increased risk of death (p = 0.09). In these patients, the risk of dying increased by 115% [HR = 2.15; 95% CI = (0.56 to 2.52)].

In conclusion, most patients with NSP (n = 52; 88.1%) had benign pleural effusion (with 11.9% being diagnosed with malignancy). Age and malignant pleural effusion were associated with the risk of death during follow-up.

A watchful-waiting strategy in NSP-patients may be appropriate although the follow up regimen is not defined. We cannot recommend a defined follow-up period, but two years could be adequate since in our study most patients had the diagnosis before two years of follow-up (57.1%).

AUTHOR CONTRIBUTIONS

ES: Study design and conception, data collection, analysis and interpretation, writing of the manuscript.

PGF, GT, BR: Data interpretation, writing of the manuscript.

CS: Data interpretation and statistical analysis.

PROTECTION OF HUMANS AND ANIMALS

The authors declare that the procedures were followed according to the regulations established by the Clinical Research and Ethics Committee and to the Helsinki Declaration of the World Medical Association updated in 2013.

DATA CONFIDENTIALITY

The authors declare having followed the protocols in use at their working center regarding patients' data publication.

COMPETING INTERESTS

ES has received payment or honoraria from Boehringer for presentation of a clinical case; also received support for attending Congresso Nacional de Pneumologia.

PGF has received consulting fees from Boehringer Ingelheim Portugal, Lda; received payment or honoraria for lectures, presentations, speakers' bureaus, manuscript writing or educational events from Boehringer Ingelheim Portugal, Lda and A. Menarini Portugal; and also received support for attending Congresso Nacional de Pneumologia

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Anemia da Doença Renal Crónica: Que Terapêuticas Estão Disponíveis?

Anemia of Chronic Kidney Disease: Which Therapeutics Are Available?

Palavras-chave: Anemia/tratamento farmacológico; Insuficiência Renal Crónica
Keywords: Anemia/drug therapy; Renal Insufficiency, Chronic

Na edição de outubro de 2022 da Acta Médica Portuguesa, foi publicado o artigo intitulado "Anemia da Doença Renal Crónica: O Estado da Arte".[1]

Trata-se de um útil artigo de revisão que aborda de forma clara e objetiva não só a fisiopatologia como também o diagnóstico e terapêutica da anemia da doença renal crónica (DRC). Contudo, face ao constante desenvolvimento de novas terapêuticas é necessário proceder a uma atualização. A 18 de agosto de 2021, o roxadustate, agente inibidor do *hypoxia-inducible factor* (HIF), foi aprovado pela European Medicines Agency e já está actualmente disponível em Portugal para tratamento da anemia na DRC. A inibição da hidroxilação da subunidade α da HIF induz a transcrição nuclear da eritropoietina, criando um ambiente de hipoxia e estimulando a produção de eritrócitos.[1] O roxadustate está disponível em farmácias comunitárias para prescrição por qualquer médico. Este fármaco ainda não foi aprovado pela Food and Drug Administration.[2] Adicionalmente, outros fármacos da mesma classe (ex.: daprodustat, vadadustat) estão ainda sob avaliação das entidades reguladoras relativamente à sua segurança e a potenciais benefícios adicionais.[3,4]

Apesar de o seu uso ainda não ser prática comum, é importante saber que está disponível para utilização e estarmos atentos a novos desenvolvimentos.[5]

CONTRIBUTO DOS AUTORES

Os autores colaboraram de igual modo na conceção do manuscrito.

CONFLITOS DE INTERESSE

Os autores declaram não ter conflitos de interesse relacionados com o presente trabalho.

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