

# ARCHIVOS DE BRONCONEUMOLOGIA

www.archbronconeumol.org

## **Original Article**

## Mortality Risk Factors in Descending Necrotising Mediastinitis

María Deu-Martín, <sup>a,\*</sup> Manel Saez-Barba, <sup>b</sup> Iker López Sanz, <sup>a</sup> Rosa Alcaraz Peñarrocha, <sup>c</sup> Laura Romero Vielva, <sup>a</sup> and Joan Solé Montserrat <sup>a</sup>

<sup>a</sup>Servicio de Cirugía Torácica, Hospital Universitario Vall d'Hebron, Barcelona, Spain <sup>b</sup>Servicio de Cirugía Maxilofacial, Hospital Universitario Vall d'Hebron, Barcelona, Spain <sup>c</sup>Unidad de Cuidados Intensivos, Hospital Universitario Vall d'Hebron, Barcelona, Spain

## ARTICLE INFO

Article history: Received November 25, 2009 Accepted January 16, 2010 Available online March 15, 2010

Keywords: Descending necrotising mediastinitis Mediastinitis Mediastinum Surgical treatment Risk factor Surgery

Palabras clave: Mediastinitis necrosante descendente Mediastinitis Mediastino Tratamiento quirúrgico Factores de riesgo Ciruzía

## ABSTRACT

*Introduction:* The term descending necrotising mediastinitis (DNM) refers to an infection that begins in the oropharyngeal region and spreads through the fascial planes into the mediastinum. This study aims to estimate the incidence of DNM in our centre, the epidemiology and clinical features of the disease and to evaluate prognostic factors influencing mortality.

*Patients and methods:* We performed a retrospective study on 43 consecutive patients diagnosed at the Hospital Universitari Vall d'Hebron in Barcelona from January 1996 to December 2006. We performed a descriptive study and a bivariate and a multivariate analysis of variables collected.

*Results:* Overall mortality was 21%, but when we subdivided the study into two periods (1996–2000 and 2001–2006) it shows a significant decrease (40% versus 4.3%). Risk factors identified in the bivariate analysis were: diagnosis period 1996–2000, diabetes mellitus, comorbidity, number of surgeries, left lateral surgery, postoperative morbidity and septic shock. In multivariate analysis, only the presence of septic shock proved to be an independent predictor of mortality.

*Conclusions:* DNM is a disease of low incidence and should be suspected clinically and confirmed immediately with a computed tomography (CT). Multidisciplinary and early treatment has allowed us to reduce mortality by 40% in the first initial period to 4.3% today.

© 2009 SEPAR. Published by Elsevier España, S.L. All rights reserved.

Archivos de

Bronconeumología

## Factores de riesgo de mortalidad en la mediastinitis necrosante descendente

## RESUMEN

*Introducción:* El término de mediastinitis necrosante descendente hace referencia a la infección que se inicia en la región orofaríngea y se disemina a través de los planos fasciales hacia el mediastino. Este trabajo tiene como objetivo estimar la incidencia de mediastinitis necrosante descendente en nuestro centro, conocer la epidemiología y las características clínicas de la enfermedad, así como evaluar los factores pronósticos que influyen en la mortalidad.

*Pacientes y métodos:* Se realiza un estudio retrospectivo de 43 pacientes consecutivos diagnosticados en el Hospital Universitari Vall d'Hebron de Barcelona desde enero de 1996 a diciembre 2006. Se efectúa un estudio descriptivo y un análisis bivariado y multivariado de las variables recogidas.

*Resultados:* La mortalidad global fue del 21%, pero al subdividir el estudio en 2 periodos (1996–2000 y 2001–06) se aprecia un importante descenso de la misma (40% vs. 4,3%). Los factores de riesgo detectados en el análisis bivariado fueron: el periodo diagnóstico 1996–2000, el antecedente de diabetes mellitus, la presencia de comorbilidad asociada, el número de intervenciones menor de 2, la lateralidad izquierda, la morbilidad postoperatoria y el choque séptico. En el análisis multivariado, sólo la presencia de choque séptico demostró ser un predictor independiente de mortalidad.

*Conclusiones:* La mediastinitis necrosante descendente es una enfermedad de baja incidencia que debe sospecharse por su clínica y confirmarse inmediatamente con la realización de una TC. El tratamiento precoz multidisciplinario nos ha permitido disminuir la mortalidad del 40% en un primer periodo inicial hasta el 4,3% actual. © 2009 SEPAR. Publicado por Elsevier España, S.L. Todos los derechos reservados.

\* Corresponding author.

E-mail address: mdeumartin@gmail.com (M. Deu-Martín).

0300-2896/\$ - see front matter © 2009 SEPAR. Published by Elsevier España, S.L. All rights reserved.

## Introduction

Head and neck infections extend to the mediastinum through the fascial spaces and the carotid sheaths. The description of the anatomical routes was made by Pearse in 1938,<sup>1</sup> who was the first to identify a group of patients whom he called "Secondary to cervical suppuration". In 1983, Estera et al<sup>2</sup> proposed the term "descending necrotising mediastinitis (DNM)", formulating criteria to include the infectious process in the DNM group: clinical evidence of severe oropharyngeal infection, compatible x-ray, verification of intraoperational or postmortem infection and the establishment of a cause-effect between oropharyngeal infection and mediastinitis.

The most common cause of DNM is odontogenic infection, followed by retropharyngeal and peritonsillar abscesses. The incidence of DNM in patients with deep neck infections is 1.5<sup>3</sup>-3.6%.<sup>4</sup> Brook and Frazier<sup>5</sup> point out that these are polymicrobial infections with anaerobic synergy of the oral cavity and Gram negative bacilli. DNM should be suspected at the onset of severe symptoms in the context of an odontogenic infection, a pharyngoamygdalitis profile or oesophageal and/or tracheal management. A cervicothoracic CT scan should be performed as soon as possible to confirm the diagnosis, since the CT scan has become the technique of choice for the diagnosis, treatment indication and follow-up of the disease.<sup>6</sup> DNM requires a multidisciplinary approach based on ICU support, aggressive antibiotic therapy and the surgical debridement of the initial infection site and the mediastinum,<sup>7</sup> since the prognosis for the disease is poor if it does not receive proper treatment: Pearse<sup>1</sup> reports 35% mortality in patients treated with surgery and 85% in patients who received only medical treatment.

The objective of our study was to evaluate the incidence of DNM in our centre, identify the clinical and epidemiological characteristics of the disease, its mortality and its risk factors.

## **Patients and Methods**

This research is based on a retrospective, descriptive and observational study that included 43 patients (23 men and 20 women) with an average age of 48 years (SD 15, range 18-79) diagnosed with DNM in the period between 01-01-1996 to 31-12-2006 at the Hospital Universitario Vall d'Hebron (University Hospital Vall d'Hebron) in Barcelona.<sup>8</sup> Once the clinical diagnosis was established, a tomographic (cervical and thoracic CT scan) study was carried out for confirmation (fig. 1). The patients were admitted to the ICU, empirical antibiotic treatment was initiated and surgical debridement was considered.

We designed a notebook to collect the data (Table 1) and performed a bivariate and multivariate analysis of the variables using the Windows<sup>®</sup> software package SPSS v. 14.0. The bivariate analysis evaluated the RR with a CI of 95% and a probability of statistical significance when less than 0.05%. The multivariate analysis was performed using multiple logistic regression, which included the variables with statistically significant differences from the bivariate study. The ORs, its 95% CI and p value are provided.

## Results

The population of the area served by our centre in relation to this pathology is around 700,000 inhabitants, by which it is calculated that the estimated annual incidence is 5.1 cases per million inhabitants. There were 31 cases of odontogenic origin, 10 cases of pharyngotonsillar origin and 2 cases of spinal origin. The average hospital stay was 39.3 days (SD 30, range 3-171). The diagnostic and therapeutic delay was 135 hours (SD 101, range 12-480).



Figure 1. Thoracic CT scan of DNM of pharyngotonsillar origin.

#### Table 1 Variables studied

valiables studied	
Demographics	Date of birth. Sex
Clinical history	BMI
	Toxic habits: smoking, alcoholism
	Diabetes mellitus
	Associated comorbidity (cardiac, pulmonary, renal and hepatic)
Diagnosis	Source of infection
	Duration from onset of condition
	Hospital stay
	Diagnostic and therapeutic delay
	CT imaging findings
	Microbiology
Treatment	Antibiotic therapy, Corticotherapy
	Surgery, number of procedures performed, laterality of the 1st
	thoracic surgery
	Length of stay in the ICU
Complications	Septic shock
	Respiratory, cardiac, renal, and hepatic failure
	Other Complications
	Sequelae
Evolution	Survival

#### Clinical History of the Study Population

Of the patients, 37.8% were non-smokers, 10.8% were ex-smokers, and 51.3% were active smokers (< 20 cig/day: 21.6%, > 20 cig/day: 29.7%). Additionally, 32% drank more than 50g of alcohol a day. They presented an average BMI of 26.7 (SD 4, range 19.6-41.8), 22 had normal weight (51%), 14 were overweight (32%), 6 were grade II-III obese (13.5%), and 1 was morbidly obese (2.9%).

There were 8 diabetic patients (18.6%) of which 5 were noninsulin dependent and 2 were insulin dependent. Comorbidity appeared in 58.4% of the cases (25 patients), which was distributed as follows: cardiac in 10 (23.3%), respiratory in 5 (11.6%), renal and/or liver in 6 (14%) and immunological abnormalities in 4 (9.3%).

## Radiographic Characteristics of Mediastinal Infection

All patients diagnosed with DNM exhibited abnormalities in the CT scan. The qualitative analysis detailed the infiltration of mediastinal fat in 51.4% of the cases, defined abscesses in 29.7% and air bubbles in 18.9%. The topographical analysis showed infection above the carina (86.5%), below the carina (5.4%), or in the entire mediastinum

sa

(8.1%). Furthermore, other anomalies were observed in the CT scan in 67.6% of the cases: unilateral pleural effusion (21.6%), bilateral pleural effusion (45.9%) and/or pericardial effusion (27%).

## Microbiology

Cultures were made for all operated patients and came back positive for 71.5% (30 cases). The germs and fungi found are listed in Table 2; the most frequent were *Streptococcus* sp. (42.7%) and mixed flora (27.8%).

## Surgical Treatment

Operations were performed on 42 of the 43 patients, with surgery ruled out for one of the patients due to multiple organ failure. Cervical debridement was performed in 94.6% of the cases and thoracic debridement in 81.1%. In addition, 40 cervicotomies, 22 right thoracotomies, 10 left and 3 bilateral were performed. The average number of interventions per patient was 3.3 (SD 1.8, range 1-9). Tracheostomy was performed in 24 cases (56.8%).

## Postoperative

Patients remained in the ICU an average of 27.8 days (SD 26, range 0-100). There were postoperative complications in 58% of the cases, of which septic shock was the most frequent and severe (table 3). Septic shock was established by the intensive care physician based on the criteria of evidence of bacterial infection, refractory hypotension upon volume treatment, the need for vasoactive drugs and metabolic acidosis.

### Mortality

Mortality was 21% (9 patients) with an average age of the deceased (50.1 years) higher than that of the survivors (46.5 years). According to the period in which the diagnosis was established, a significant

Table 2   Organisms found in positive cultures	
Bacteroides sp.	Fusobacterium avium
Candida albicans	Peptostreptococcus
Clostridium difficile	Prevotella sp.
Eikenella corrodens	Gemella morbillorum
Enterococcus faecalis	Propionibacterium sp.
Escherichia coli	Pseudomona aerugino
	Streptococcus sp.
	S. Acidominimus
	S. Anginosus
	S. Pyogenes
	S. Viridans

## Table 3

Postoperative complications

Complication	Number of patients	%
Septic shock	10	23.3
Heart failure	3	7
Renal and/or hepatic failure	6	14
Other	10	23.3
High digestive haemorrhage	4	9.3
Cholecystitis	2	4.6
Intestinal perforation	1	2.3
Stroke	1	2.3
Seizure	2	4.6

decrease was observed when comparing the results of the last group with those of the first (4.3% versus 40% of the initial period).

#### Bivariate and Multivariate Analysis of Mortality Risk Factors

The diagnostic period 1996-2000, a history of diabetes mellitus, the presence of associated comorbidity, a number of interventions below 2, left laterality and septic shock were the variables that were related with mortality in the bivariate analysis (Table 4). The only independent predictor of mortality in the multivariate analysis was septic shock (Table 5).

## Discussion

DNM is a rare infectious process in our environment that is difficult to diagnose and whose therapy is openly debated. The literature contains numerous questions about various aspects of the problem: risk factors involved in its appearance, strategies for diagnosis and treatment, factors that influence its mortality, etc. There is controversy about each of these points and each new article, which always covers few cases, attempts to provide some input even though only a few offer the multivariate analyses that are necessary for determining risk factors. Our study is the largest series that exists in the Spanish literature and has allowed for a bivariate and multivariate analysis.

The incidence of DNM in our environment and during the study period was 5.1 cases per 1,000,000 inhabitants/year. One should keep in mind that this is a retrospective study in which incidence tends to be undervalued, although we believe that this would produce only a small bias since the data has been collected and compared from various sources. This low incidence is similar to that of the few published series. The authors describe a decreasing incidence over the last thirty years, after the improvement of buccopharyngeal hygiene in developed countries and the introduction of new antibiotics.<sup>2</sup>

In our casuistics, DNM appeared with greater frequency in males in their fifties. The Ridder et al<sup>9</sup> series and the Cirino et al<sup>10</sup> and Wheatley et al<sup>11</sup> reviews of the English literature also note a greater incidence in males, although of a younger age, while the Hirai et al<sup>12</sup> review of the Japanese series shows a greater incidence in more advanced ages.

The most frequent cause of DNM in our series was an odontogenic origin, similar to the Cirino et al<sup>10</sup> and Wheatley et al<sup>11</sup> reviews, and the Mora et al<sup>13</sup> series. In contrast, Hirai et al<sup>12</sup> observed an increased incidence of cervical infections. It should be remembered, however, that since the review of the latter is done on Japanese literature, it is possible that the oral hygiene habits of the population, the various applied antibiotic treatments and their resistance in such disparate geographical areas may cause discrepancies. We cannot rule out an observational bias either, since Makeieff et al,<sup>14</sup> from an otorhinolaryngology department, present a series of 17 patients of which 13 were of pharyngeal and 6 of odontogenic origin. None of the articles reviewed presented more than 2 cases of DNM of osteoarticular origin, as with our series.

Hospital stays tend to be long (39.3 days, SD 30, range 3-171) and the majority of the time in hospital consists of stays in the ICU (27.8 days, SD 26, range 1-100), which is similar to what is reported in the literature.<sup>14</sup> This figure corresponds to the current concept of strict monitoring and support treatment that this pathology requires.

Another important figure to consider is the diagnostic-therapeutic delay. In our series, this delay was 135 hours (DS 101, range 12-480), which is consistent with the literature<sup>13,14</sup> and is related to the difficulties in clinical diagnosis.

With regard to toxic habits, half of the patients in the series were active smokers (in Spain, 35% of the population over 16 are smokers<sup>15</sup>)

Table 4

Bivariate analysis

Bivariate analysis Variable	Exitus	Alive	RR	CI 95%	Р
	Exitus	711170	int	CI 5570	
Age < 66 years	6	30	0.73	0.45-1.17	0.06
$\geq$ 66 years	3	4	3.66	0.88-15.1	0.00
Sex					
Male	6	17	1.29	0.73-2.28	0.41
Female	3	17	0.68	0.25-1.84	
Diagnostic period	0	10	2.44	1 47 4 05	0.005
1996-2000 2001-2006	8 1	12 22	2.44 0.17	1.47-4.05 0.02-1.12	0.005
Smoking habit		22	0.17	0.02 1.12	
< 20 pack years	7	24	1.06	0.71-1.60	0.76
> 20 pack years	2	10	0.51	0.21-3.12	
Alcohol habit:					
< 50g/day	8	23	1.33	0.95-1.86	0.19
> 50g/day BMI	1	11	0.33	0.04-2.25	
< 30	6	28	0.81	0.50-1.32	0.32
≥ 30	3	6	1.83	0.56-5.92	0.012
Diabetes mellitus					
No	4	30	0.48	0,23-1,02	0.002
Yes (DMNID/DMID)	5	4	4	1.79-20.84	
Associated comorbidity					
No Yes	1 8	22 12	0.16 2.66	0.02-1.07 1.56-4.55	0.003
Cardiac comorbidity	0	12	2.00	1.30-4.33	
No	5	27	0.67	0.37-1.24	0.10
Yes	4	7	2.44	0.87-6.83	
Pulmonary comorbidity					
No	6	31	0.71	0.44-1.13	0.02
Yes	3	3	5.5	1.07-28.0	
Renal/hepatic comorbidity No	8	28	1.04	0.79–1.37	0.75
Yes	8 1	6	0.73	0.79-1.37	0.75
Immune disorders	•	0	0175	0100 0100	
No	8	30	0.97	0,75-1.26	0.85
Yes	1	4	1.22	0.14-10.38	
Therapeutic delay	2	0	0.01	0.01 0.10	0.70
< 72 h > 72 h	2 7	9 23	0.81 1.06	0.21-3.12 0.71-1.60	0.76
CT scan characteristics	1	23	1.00	0.71-1.00	
Infiltration	6	17	1.29	0.73-2.28	0.41
Abscess/air	3	17	0.68	0.25-1.84	
CT extension					
Above carina	8	29	1.04	0.79-1.37	0.75
Below carina/all Pleural effusion	1	5	0.73	0.09-5.50	
No	2	11	0.66	0.17-2.48	0.52
Yes	7	23	1.16	0.76-1.78	
Pericardial effusion					
No	5	22	0.87	0.46-1.65	0.65
Yes	4	12	1.22	0.51-2.88	
Culture Negative	1	10	0.36	0.05-2.49	0.24
Positive	8	24	1.27	0.92-1.76	0.24
Number of interventions					
1	5	5	3.66	1.35-9.93	0.01
> 1	4	28	0.52	0.24-1.10	
Laterality 1st SI	2	26	0.42	0.16 1.00	0.000
Right	3 6	26 7	0.42 3.14	0.16-1.08	0.009
Left Postsurgical complications	0	7	5.14	1.40-7.02	
No	4	26	0.58	0.27-1.24	0.07
Yes	5	8	2.36	0.99-5.30	
Septic shock					
No	3	30	0.37	0.14-0.96	0.001
Yes	6	4	5.50	1.96-15.3	

and 32% were drinking more than 50g of alcohol a day (the prevalence of alcoholism in Spain is 15%<sup>15</sup>), especially in the case of males (46%).

I	a	bl	le	5			
n	π.	.1			:	- 4	

Multivariate	analysis

	OR	CI 95%	Р
Diagnostic period	0.23	0.03-1.08	0.06
Diabetes mellitus	5.48	0.41-66.62	0.16
Comorbidity	0.21	0.006-4.87	0.35
Laterality of 1 <sup>st</sup> intervention	2.12	0.33-11.78	0.39
Number of interventions	0.42	0.16-1.29	0.09
Septic shock	48.2	4.38-542.21	0.002

The series featured BMIs greater than that of the Spanish population, according to the SEEDO 2000 study on the prevalence of obesity in Spain,<sup>16</sup> which corroborates the correlation between obesity and the tendency towards infection that has been observed in other pathologies.<sup>17</sup>

Among the patients, 19% were diabetics (the prevalence of diabetes mellitus in adults in our area is 10.3%<sup>18</sup>), similar to that reflected in the Hirai et al review<sup>12</sup> (23%). A large number of studies with patients undergoing heart surgery reported an increased risk of mediastinitis in diabetic patients.<sup>17</sup> These studies analysed the factors that confer vulnerability to the infection such as hyperglycaemia, diabetes, diabetic vasculopathy or a decrease in the inflammatory response that diabetic patients present, without having reached any conclusion. Additionally, 58.4% of the patients presented associated comorbidity (chronic obstructive pulmonary disease, cancer, cardiopathy and at a lower percentage, renal and liver failure and immunological disorders).

The CT scan is essential both to establish the diagnosis and for follow-up. All of series' patients presented disorders in the CT scan and an average of 3.6 explorations had to be performed, a figure similar to that indicated by other authors.<sup>19</sup> The same observations were made, mainly the presence of fat infiltration and abscesses, as in the Exarhos et al<sup>20</sup> series. In terms of pathways of propagation, the extension of infection was predominantly cervical (86.5%). As with the Misthos et al<sup>7</sup> and Makeieff et al<sup>14</sup> series, the CT scan also allowed us to catalogue pleuropericardic injuries, of which the most common were pleural effusion (67%) and pericardial effusion (27%).

As for isolated microbial flora, the cultures were positive in 71.5% of the cases. This data coincides with the Makeieff et al series,<sup>14</sup> which noted 17% negative cultures. This is possibly due to the early use of antibiotics that were administered at the time of the suspected diagnosis. The organisms obtained most frequently were *Streptococcus* sp. The cultures were polymicrobial and aerobic/anaerobic in 75% of the cases. Various authors<sup>5,9,14,21</sup> performed the microbiological analysis in different series and obtained data similar to ours. Brook and Frazier<sup>5</sup> also demonstrated the importance of performing anaerobic cultures by isolating an average of 2.5 species in each sample: 0.8 aerobic and 1.7 anaerobic.

The treatment was initiated with empirical antibiotic therapy that covered the mixed aerobic/anaerobic flora described in the literature,<sup>5</sup> subsequently adapting it according to the antibiogram. Surgical debridement was performed in 42 of the 43 patients diagnosed. The patient who was not operated on died of multiple organ failure despite non-surgical multidisciplinary treatment. The average number of procedures performed was 3.3 (SD 1.8) similar to the Ridder et al series.9 Cervical debridement and thoracotomy were the most frequent means of debridement, although anterior laparotomies and mediastinotomies were also performed. No mediastinoscopies or thoracoscopies were performed as they are not considered appropriate in any case. These data are similar to those of Wheatley et al<sup>11</sup> and Makeieff et al.<sup>14</sup> The results of Misthos et al<sup>7</sup> and the meta-analysis of Corsten et al<sup>22</sup> support our decision to perform thoracotomies since they achieve a 91% survival rate when a debridement is performed by means of a cervicotomy and

thoracotomy, and a 50% mortality rate when only a cervicotomy is performed. Whenever possible a right thoracotomy was chosen. An approach from the left side was only performed in cases of left predominant pathology since debridement by this route is complicated by the location of the heart, the aortic arch and the descending aorta. In patients with cervical oedema in whom a difficult intubation is predicted, an early tracheotomy has been steadily dropped over the twelve years of the study in favour of an intubation by means of fibrobronchoscopy with the patient awake. The current literature considers that tracheostomy facilitates the aspiration of pus and the spread of infection to the anterior mediastinum and thus contributes to the persistence of cervical and mediastinal sepsis.<sup>12,13</sup>

Septic shock was the most common postoperative complication in our series (23.3%). Ridder et al<sup>9</sup> observed septic shock in 31% of their patients and both Misthos et al<sup>7</sup> and Makeieff et al<sup>14</sup> refer to a septic shock index greater than 50% in their results and confirm a high risk of heart, renal, and respiratory complications. The high frequency with which these complications arise requires continuous monitoring through admission to an ICU. Patients who survived the disease process presented sequelae in 16% of cases, a figure somewhat lower than that reflected by Makeieff et al.<sup>14</sup>

Mortality in our series was 21% but it should be noted that there was a significant drop from 40% initially to 4.3% currently (the revised series also show this trend, as seen in Table 6).

The bivariate analysis conducted on the study to establish risk factors for mortality indicated the following variables as statistically significant: diagnostic period 1996-2000, history of diabetes mellitus, presence of associated comorbidity, number of interventions less than 2, left laterality and septic shock. There was no statistical significance for the rest of the variables.

Age and sex were not statistically significant risk factors (p = 0.06 and p = 0.41, respectively), although age shows an effect. However, in the Cirino et al<sup>10</sup> review, higher mortality was observed in patients older than 70 years of age.

We have already noted that patients diagnosed in the first six years of study had a higher risk of mortality (p = 0.005) than those who were diagnosed in the period 2000-2006. This decrease may be related to increased diagnostic surveillance that has been maintained in our centre in recent years in patients with odontogenic abscesses and/or pharyngoamygdalitis where an early cervicothoracic CT scan allowed for diagnosis without delay (delay for period 1996-2000: 147 h delay for period 2001-2006: 103 h). This decrease is also attributable to the multidisciplinary treatment implemented in this latter period that included: admission to the ICU; empirical antibiotic treatment; haemodynamic, respiratory and nutritional support from the moment of admission; and early and aggressive surgical treatment.

Smoking (p = 0.76) and drinking (p = 0.19) were not risk factors for mortality. We have not found series in the literature that assess the relationship between toxic habits and mortality risks in DNM.

Obesity was not a predictor of mortality in our series either (p = 0.32) in contrast to what occurred in studies performed on poststernotomy mediastinitis where it acted as a risk factor.<sup>23</sup> According to these studies, obesity would imply insufficient levels of antibiotics due to under-dosage and poor perfusion in the adipose tissue and added surgical difficulties with increased surgical time. This discrepancy with the literature is possibly due to the small number of obese patients in our series, although the adjustment of the antibiotic treatment performed on these patients may have also played an important role.

The diabetic patients showed a statistically significant (p = 0.002) higher mortality risk than the non-diabetics. Bross-Soriano et al<sup>24</sup> also observed increased mortality in diabetic patients in their series of 121 patients with Ludwig's angina, as did the Cirino et al<sup>10</sup> review on DNM and poststernotomy mediastinitis after cardiac surgery.<sup>25</sup>

#### Table 6

Mortality in	historical	series
--------------	------------	--------

Year	Author	Mortality	Number of cases
1938	Pearse <sup>1</sup>		
	Without debridement	86%	110 (11 initial+99 review)
	With debridement	35%	
1983	Estrera et al <sup>2</sup>	43%	10
1999	Marty-Ane et al <sup>1</sup>	16.5%	12
2000	Freeman et al <sup>19</sup>	0%	10 initial
		29%	96 review
2004	Makeieff et al <sup>14</sup>	17.5%	17
2007	Misthos et al <sup>7</sup>	33.3%	27 DNM anterior
	Cervicotomy + thoracotomy	9%	11
	Cervicotomy + transcervical drainage	50%	16
2009	Ridder et al <sup>9</sup>	11.1%	45

Because hyperglycaemia is a modifiable variable and although it is not known whether the risk is directly related to hyperglycaemia or with the general diabetic state, an adjustment in glucose levels should be performed in all patients diagnosed with DNM at the time of admission. In this way, we try to reduce this risk factor as much as possible, as has been done in other pathologies.<sup>26</sup> General comorbidity was also statistically significant (p = 0.003) at the expense of pulmonary comorbidity (p = 0.02). Cardiac comorbidity (p = 0.10), renal/hepatic comorbidity (p = 0.75), and immunological disorders (p = 0.85) were not statistically significant.

Although most authors suggest a predictive factor for diagnostictherapeutic delay, a delay greater than 72 hours was not a mortality factor in our series (p = 0.76). Perhaps the cut-off point was not correct, although Misthos et al<sup>7</sup> presented a study where the multivariate analysis only provided differences in relation to aggressive surgical treatment and not to the delay.

Qualitative characteristics (p = 0.41) and extension (p = 0.75) in the CT scan were not statistically significant. Neither pleural effusion (p = 0.52), which is very common in DNM, nor pericardial effusion (p = 0.65) were significant. There are no series that discuss the importance of pleural or pericardial effusion in DNM.

The microbiological culture was not a prognostic factor (p = 0.24) in our series. The Brook and Frazier<sup>5</sup> studies are descriptive but do not have ratings on the risk of mortality.

The variable "number of interventions" was statistically significant (p = 0.01). Patients who had been operated on more than one occasion had a better prognosis than those who had only been operated on once. This figure is possibly related to the difficulties in maintaining a continuous drainage after debridement and the removal of necrotic tissue, for which surgical revisions seem to be required. The only prognostic factor in the multivariate study by Misthos et al<sup>7</sup> was aggressive and repeated surgical treatment in case of persistent pathology.

Patients who were operated on the right side during the first surgery had a significantly better prognosis (p = 0.009) than those in which the first thoracotomy was performed on the left. Right thoracotomy with ligation of the arch of the azygos vein and extensive debridement of the entire mediastinum provides better access than the left thoracotomy where the heart and the aorta hinder debridement and removal of necrotic tissue as well as hinder drainage of the abscesses, which tend toward septation.

The occurrence of postoperative renal, hepatic, cardiac or respiratory failure was not a statistically significant factor for bad prognosis in our series, although it did show a tendency (p = 0.07). In contrast, the presence of septic shock after initial treatment was one of the risk factors in the bivariate analysis (p = 0.001) and the only statistically significant risk factor in the multivariate analysis (p = 0.001)

0.002). The occurrence of septic shock is the result of therapeutic delay, incorrect antibiotic therapy and insufficient debridement, and correlates with high mortality in our series.

## Conclusions

DNM is a low-incidence disease in our environment, but it should be suspected based on clinical symptoms and confirmed quickly with a CT scan. Its treatment must be multidisciplinary and aggressive since this approach achieves a decrease in its mortality.

## **Conflicts of Interest**

The authors affirm that they have no conflicts of interest.

## References

- 1. Pearse HE. Mediastinitis following cervical suppuration. Ann Surg. 1938;108: 580-611.
- Estrera AS, Landay MJ, Grisham JM, Sinn DP, Platt MR. Descending necrotizing mediastinitis. Surg Gynecol Obstet. 1983;157:545-52.
- Crespo AN, Chone CT, Fonseca AS, Montenegro MC, Pereira R, Milani JA. Clinical versus computed tomography evaluation in the diagnosis and management of deep neck infection. Sao Paulo Med J. 2004;122:259-63.
- Boscolo-Rizzo P, Marchiori C, Montolli F, Vaglia A, Da Mosto MC. Deep Neck Infections: A Constant Challenge. ORL J Otorhinolaryngol Relat Spec. 2006;68:197-203.
- 5. Brook I, Frazier EH. Microbiology of mediastinitis. Arch Intern Med. 1996;156:333-6.
- 6. Scaglione M, Pinto A, Romano S, Giovine S, Sparano A, Romano L. Deep Neck Infections: A Constant Challenge. Emerg Radiol. 2005;11:275-80.
- Misthos P, Katsaragakis S, Kakaris S, Theodorou D, Skottis I. Descending necrotizing anterior mediastinitis: analysis of survival and surgical treatment modalities. J Oral Maxillofac Surg. 2007;65:635-9.
- 8. Deu Martín M. Factores de riesgo de mortalidad en la mediastinitis aguda. Doctoral Thesis: Universitat Autònoma de Barcelona; 2008.
- Ridder GJ, Maier W, Kinzer S, Teszler C, Boedeker C, Pfeiffer J. Descending necrotizing mediastinitis. Conttemporary trends in etiology, diagnosis, management and outcome. Ann Surg. 2009. [Epub ahead of print]
- Cirino LM, Elias FM, Almeida JL. Descending mediastinitis: a review. Sao Paulo Med J. 2006;124:285-90.

- Wheatley MJ, Stirling MC, Kirsh MM, Gago O, Orringer MB. Descending necrotizing mediastinitis: Transcervical drainage is not enough. Ann Thorac Surg. 1990;49: 780-4.
- Hirai S, Hamanaka Y, Mitsui N, Isaka M, Mizukami T. Surgical treatment of virulent descending necrotizing mediastinitis. Ann Thorac Cardiovasc Surg. 2004;10:34-8.
- Mora R, Jankowska B, Catrambone U, Passali GC, Mora F, Leoncini G, et al. Descending necrotizing mediastinitis: ten years' experience. Ear Nose Throat J. 2004;83:774-80.
- Makeieff M, Gresillon N, Berthet JP, Garrel R, Crampette L, Marty-Ane C, et al. Management of descending necrotizing mediastinitis. Laryngoscope. 2004; 114:772-5.
- Ministerio de Sanidad y Consumo. Encuesta domiciliaria sobre alcohol y drogas en España (EDADES), 2005–2006. http://www.msc.es/gabinetePrensa/notaPrensa/ pdf/GraficosEncuestaDrogas.ppt
- Aranceta J, Serra L, Foz M, Moreno B, y Grupo colaborativo para el Estudio de la Obesidad en Espana. Prevalencia de la obesidad en España. Med Clin (Barc). 2005;125:460-6.
- Diez C, Koch D, Kuss O, Silber RE, Friedrich I, Boergermann J. Risk factors for mediastinitis after cardiac surgery – a retrospective analysis of 1700 patients. J Cardiothorac Surg. 2007;2:23.
- Castell C, Tresserras R, Serra J, Goday A, Lloveras G, Salleras L. Prevalence of diabetes in Catalonia (Spain): an oral glucose tolerance test-based population study. Diabetes Res Clin Pract. 1999;43:33-40.
- Freeman RK, Vallieres E, Verrier ED, Karmy-Jones R, Wood DE. Descending necrotizing mediastinitis: An analysis of the effects of serial surgical debridement on patient mortality. J Thorac Cardiovasc Surg. 2000;119:260-7.
- Exarhos DN, Malagari K, Tsatalou EG, Benakis SV, Peppas C, Kotanidou A, et al. Acute mediastinitis: spectrum of computed tomography findings. Eur Radiol. 2005;15:1569-74.
- Inoue Y, Gika M, Nozawa K, Ikeda Y, Takanami I. Optimum drainage method in descending necrotizing mediastinitis. Interac Cardiovasc Thorac Surg. 2005;4: 189-92.
- 22. Corsten MJ, Shamji FM, Odell PF, Frederico JA, Laframboise GG, Reid KR, et al. Optimal treatment of descending necrotising mediastinitis. Thorax. 1997;52: 702-8.
- 23. Molina JE, Lew RS, Hyland KJ. Postoperative sternal dehiscence in obese patients: incidence and prevention. Ann Thorac Surg. 2004;78:912-7.
- Bross-Soriano D, Arrieta-Gomez JR, Prado-Calleros H, Schimelmitz-Idi J, Jorba-Basave S. Management of Ludwig's angina with small neck incisions: 18 years experience. Otolaryngol Head Neck Surg. 2004;130:712-7.
- Guvener M, Pasaoglu I, Demircin M, Oc M. Perioperative hyperglycemia is a strong correlate of postoperative infection in type II diabetic patients after coronary artery bypass grafting. Endocr J. 2002;49:531-7.
- Carr JM, Sellke FW, Fey M, Doyle MJ, Krempin JA, de la Torre R, et al. Implementing tight glucose control after coronary artery bypass surgery. Ann Thorac Surg. 2005;80:902-9