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Sarcopenia is predictive of nosocomial infection in care of the elderly

Gaëlle Cosquéric[1], Aline Sebag[2], Cyril Ducolombier[1], Caroline Thomas[3], François Piette[1] and Sébastien Weill-Engerer[1]*

[1]*Service de gériatrie, hôpital Rothschild, Assistance Publique – Hôpitaux de Paris, Paris, France*
[2]*Service de radiologie, hôpital Rothschild, Assistance Publique – Hôpitaux de Paris, Paris, France*
[3]*Service de gériatrie, hôpital Saint Antoine, Assistance Publique – Hôpitaux de Paris, Paris, France*

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Protein–energy malnutrition and nosocomial infection (NI) are frequent in elderly patients, and a causal link between the two has often been suggested. The aim of the present study was to identify the nutritional parameters predictive of NI in elderly patients. We assessed on admission 101 patients (sixty-six women, thirty-five men, aged over 65 years) admitted to an acute care of the elderly department. Sarcopenia was detected by dual-energy X-ray absorptiometry, with appendicular skeletal muscle mass expressed with respect to body area. Weight, BMI, albuminaemia, serum transthyretin and C-reactive protein values were also determined on admission, and known risk factors, such as functional dependence and invasive biomedical material, were also evaluated. After up to 3 weeks of hospitalisation, patients were classified according to whether they had developed an NI. After 3 weeks of hospitalisation, we found that twenty-nine patients had suffered an NI, occurring after a mean of 16·1 d. Patients who were sarcopenic on admission had a significantly higher risk of contracting an NI (relative risk 2·1, 95 % CI 1·1, 3·8). None of the other morphometric or biological parameters differed significantly between the two groups of patients on admission. Patients who experienced an NI were also more likely, on admission, to have a medical device ($P=0·02$ to $P=0·001$ depending on the device), to have swallowing problems ($P=0·002$) or to have restricted autonomy ($P<0·01$). Sarcopenia on admission to an acute care of the elderly unit, as measured by X-ray absorptiometry, was therefore associated with a doubled risk of NI during the first 3 weeks of hospitalisation.

Protein–energy malnutrition: Aged: Frail elderly: Nosocomial infection: Sarcopenia

The prevalence of nosocomial infection (NI) in industrialised countries is between 6 % and 19 % (EPINE Working Group, 1992; Emmerson *et al.* 1996; Gastmeier *et al.* 1998; Scheel & Stormark, 1999; Vaque *et al.* 1999; French Prevalence Survey Study Group, 2000; Klavs *et al.* 2003; Gikas *et al.* 2004), and the prevalence of NI is about three times higher in patients over the age of 80 years (Saviteer *et al.* 1988; Hussain *et al.* 1996; Klavs *et al.* 2003).

The frequency, gravity (particularly in elderly patients) and cost of NIs have made these infections a major public health problem. Prevention, by identifying and combatting risk factors, is therefore of prime importance. Certain risk factors have already been identified. They include intrahospital or interhospital transfer, length of stay in hospital, invasive devices and care manoeuvres, and certain types of organ failure (such as kidney failure or chronic respiratory failure), diabetes, immunodepression (particularly if induced by treatment), neoplasm, loss of autonomy, urinary incontinence, swallowing difficulties, sequelae of cerebral vascular accidents and problems with alertness (Harkness *et al.* 1990; Michel *et al.* 1991; Hanson *et al.* 1992; Cunnion *et al.* 1996; Hussain *et al.* 1996; Kampf *et al.* 1997; Wischnewski *et al.* 1998; Pittet *et al.* 1999; Klavs *et al.* 2003; Rothan-Tondeur *et al.* 2003; Gikas *et al.* 2004). It has not yet been determined whether age is an associated factor or a truly independent risk factor.

Protein-energy malnutrition (PEM) is also frequently observed in hospitalised patients. In elderly patients hospitalised for short periods or in aftercare, the prevalence of PEM is between 10 % and 40 % (Pinchcofsky & Kaminski, 1985; Constans *et al.* 1992; Mowe *et al.* 1994; Dormenval *et al.* 1995).

It is widely thought that there is a risk of NI in patients with PEM, for two principal reasons: PEM has been shown to lead to a decrease in immunity (Lipschitz & Udupa, 1986; Chandra, 1992; Good & Lorenz, 1992; Mazari & Lesourd, 1998; Lesourd & Mazari, 1999; Cederholm *et al.* 2000), and several studies have reported a significant relationship between NI and BMI, albuminaemia or cutaneous folds and brachial circumference (Bienia *et al.* 1982; Michel *et al.* 1991; Hanson *et al.* 1992; Potter *et al.* 1995; Rothan-Tondeur *et al.* 2003; Schneider *et al.* 2004). These studies reported differences in nutritional markers at the time of the NI, but differences before the occurrence of the NI, which would have had predictive value, were not described. Albuminaemia is neither specific nor sensitive for malnutrition (Klein, 1990; Reuben *et al.* 1995; Rosenthal *et al.* 1998; Omran & Morley, 2000), whereas the calculation of BMI and measurement of skin folds are simple, useful and widely used, but unable to provide an accurate estimate of body composition (Lemonnier *et al.* 1991; Kyle *et al.* 2001).

Abbreviations: ASM, appendicular skeletal muscle mass; DEXA, dual X-ray absorptiometry; NI, nosocomial infection; PEM, protein–energy malnutrition.

* **Corresponding author:** Dr Sébastien Weill-Engerer, fax +33 1 40 19 33 64, email sebastien.weill-engerer@rth.aphp.fr

The aim of this study was to determine whether markers of malnutrition, and sarcopenia, diagnosed by dual-energy X-ray absorptiometry (DEXA) are risk factors predictive of NI in care of the elderly.

Materials and methods

Study population

The subjects included in this study were consecutive patients (men or women), over the age of 65 years, admitted to an acute care of the elderly ward. The exclusion criteria were life expectancy of less than 1 month, infection on admission, motor agitation, the patient being untransportable, disturbed water metabolism (dehydration, oedema), symmetrical joint replacements in the legs (which would affect DEXA readings) and refusal to undergo examination.

The most commonly identified diseases in overall patients of the study were kidney failure, heart failure and dementia (Table 1). One case of liver failure and one case of haemopathy were observed. Seven patients in the non-NI group were treated with corticosteroids.

The study

Data were collected prospectively in a cohort of elderly patients. The following data were collected on admission: active diseases, degree of autonomy (assessed on the basis of a five-item score derived from Katz's scale (Katz *et al.* 1963)), body temperature, anthropometric data (weight, height calculated from knee height (Chumlea *et al.* 1985), BMI) and biological data (C-reactive protein concentration, albuminaemia, serum transthyretin concentration).

We assessed possible sarcopenia on admission by DEXA (Lunar Prodigy; GE Medical Systems Europe, Buc, France), during routine screening for osteoporosis, systematically carried out in this high-risk population. Sarcopenia was defined according to the criteria of Baumgartner *et al.* as modified by Newman *et al.* based on the ratio of appendicular skeletal muscle mass (ASM) to body area (height^2). Sarcopenia was defined as an ASM:height^2 ratio below 5·45 kg/m^2 in women and below 7·26 kg/m^2 in men (Baumgartner *et al.* 1998; Newman *et al.* 2003). Weight, BMI, albuminaemia and serum transthyretin concentration were considered as secondary criteria for this study. Patients were considered to present malnutrition if they had a BMI below 20 kg/m^2, albuminaemia below 35 g/l or a serum transthyretin concentration below 150 mg/l (Pinchcofsky & Kaminski, 1985; Constans *et al.* 1992; McWhirter & Pennington, 1994; Mowe *et al.* 1994; Dormenval *et al.* 1995; Edington *et al.* 2000).

We followed all patients during their hospital stay for a period of up to 3 weeks, recording all cases of NI. An infection was considered to be nosocomial if it occurred during the patient's stay in hospital and began at least 48 h after admission. Infections were confirmed on the basis of the criteria for probable or certain infection of the Centers for Disease Control (Garner *et al.* 1988), as modified by the Comité de Lutte contre les Infections Nosocomiales de l'Assistance Publique – Hôpitaux de Paris for application to a population with few spontaneous infections and in whom invasive bacteriological investigations are not systematically carried out (Cassou & Rothan-Tondeur, 2000). These diagnoses involved additional imaging and biochemical or bacteriological testing in some cases. Patients not meeting the criteria for NI were considered to belong to the 'non-NI' group. Patients were recruited prospectively in order to achieve the number needed regarding the power estimate (hypergeometric sampling).

Table 1. Comparison of characteristics and diseases on admission (excluding nutritional parameters) between the two groups of patients identified at the end of the study

	NI group (*n* 29)		Non-NI group (*n* 72)		
	Mean or prevalence	SD	Mean or prevalence	SD	*P*
Age (years)	85·8	5·7	85·2	6·9	0·64
Female (%)	55·2 %		69·4 %		0·25
Number of drugs taken	5·9	3·2	5·3	2·6	0·30
Autonomy (/5)	1·9	1·3	2·8	1·3	0·006
Kidney failure	55·2 %		43·1 %		0·28
Heart failure	34·5 %		29·2 %		0·64
Diabetes	10·3 %		15·3 %		0·75
Dementia syndrome	51·7 %		62·5 %		0·37
Swallowing problems	20·7 %		1·4 %		0·002
Nasogastric probe	10·3 %		0 %		0·02
Urinary probe or subpubic catheter	41·4 %		6·9 %		0·0001
Peripheral venous catheter	62·1 %		22·2 %		0·0003

NI, nosocomial infection

Ethics

ASM:height^2 measures were obtained by DEXA during systematic measurements of bone density, which were themselves carried out according to the indications and recommendations of the Agence Nationale d'Evaluation et d'Accréditation en Santé. This study complied with the Helsinki Declaration. Only the clinical and paraclinical data collected in the patients' medical files during their hospitalisation and the usual procedures of the department were used in this study.

Statistics

This study was designed to make it possible to demonstrate a significant difference of 10 % in ASM:height^2, with an α risk of 5 % and a β risk of 5 %. Few reference values are available from previous studies, but the mean value of ASM:height^2 for women has been estimated to be 6·33 $\pm$ 0·78 kg/m^2 (Gillette-Guyonnet *et al.* 2003). Given the predictable imbalance in the sizes of the NI and non-NI groups, we estimated that twenty-nine patients were required for the NI group and seventy-two for the non-NI group for a significant effect to be detected.

We used Fisher's exact test to search for a link between the occurrence of NIs and the various nominal variables. We used Student's *t* tests for independent variables to search for a link between the occurrence of NIs and continuous numerical parameters. The results are presented as means and standard deviations unless otherwise specified. The threshold of significance was set at 5 %.

Results

We analysed the data for the 101 patients who did not meet the exclusion criteria. At the end of their stay in hospital, or no more than 3 weeks after admission, twenty-nine of these patients had suffered a probable or certain NI. The other seventy-two patients were included as non-NIs. In the NI group, infection occurred an average of 16·1 (SD 8·9) d after admission. The infections observed were primarily bronchopulmonary (44·8 %) or urinary (34·5 %). Seven patients in the NI group died, and four of these deaths were directly attributable to the infection. No deaths were recorded in the non-NI group (Fisher exact test comparing the seven to zero deaths, $P<0·0001$).

The NI and non-NI groups did not differ significantly in terms of sex ratio or age (Table 1). The number and type of diseases identified in the two groups at admission were similar, except for swallowing problems (20·7 % in the NI group *v.* 1·4 % in the non-NI group; $P=0·002$). Based on the mean serum transthyretin concentration (165 mg/l) and mean albuminaemia (30·4 g/l), the subjects studied (NI and non-NI) displayed only slight or moderate malnutrition. The BMI values recorded for the women (24·6 kg/m^2) and for the men (23·4 kg/m^2) on admission were similar to or only moderately lower than the values for the non-hospitalised, healthy population (Gillette-Guyonnet *et al.* 2003; Newman *et al.* 2003). On admission, the two groups did not differ significantly in terms of body temperature (37·3 (SD 0·8) °C in the NI group *v.* 37·1 (SD 0·5) °C in the non-NI group) or C-reactive protein concentration (geometric means 15·4 in the NI group *v.* 10·8 in the non-NI group; *z*-test for log C-reactive protein: $P=0·3$).

The proportion of patients with an invasive device on admission (nasogastric probe, urinary probe, subpubic or venous catheter) – a known risk factor for NI – was higher in the NI group than in the non-NI group (69·0 % *v.* 26·4 %; $P=0·0001$), and the NI group was significantly less autonomous (1·9 (SD 1·3) *v.* 2·8 (SD 1·3); $P=0·006$).

The proportion of patients who were sarcopenic on admission was twice as high in the NI group as in the non-NI group (44·8 % *v.* 21·1 %; $P=0·03$; Fig. 1), this effect being largely due to the subgroup of women. Therefore, the relative risk of NI in the first 3 weeks of hospitalisation associated with sarcopenia on admission was 2·1 (95 % CI 1·1, 3·8). However, ASM:height^2 at admission did not differ significantly between the two groups (6·8 *v.* 6·9 kg/m^2; Table 2). The significant difference between the percentages of sarcopenic patients in the two groups, with no difference in mean ASM:height^2, is accounted for by an asymmetrical ASM:height^2 distribution in the NI group (Fig. 2). This difference was not due to an imbalance in the number of men and women between the two groups, because the proportion of women did not differ significantly between the two groups.

Albuminaemia tended to be lower on admission in patients who went on to develop an NI, but this difference was not significant ($P=0·07$). The other nutritional parameters (weight, BMI, serum transthyretin) did not differ significantly between the two groups ($P=0·63$, $P=0·68$, $P=0·15$, respectively). Nor did the proportion of patients considered to be suffering from malnutrition according to BMI, albuminaemia or serum transthyretin concentration differ between the two groups ($P=0·29$, $P=0·38$, $P=0·27$, respectively).

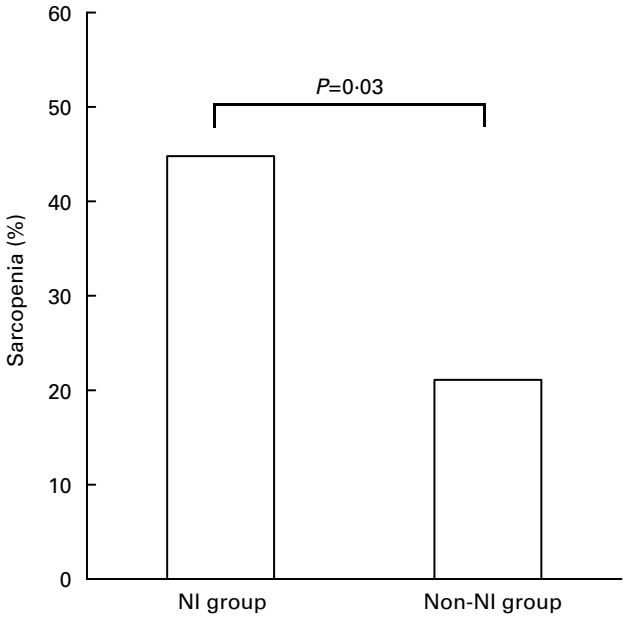

Fig. 1. Prevalence of sarcopenia on admission among patients subsequently presenting nosocomial infection (NI group) or no such infection (non-NI group) during their hospital stay.

Discussion

This study is the first to demonstrate that sarcopenia, measured on admission to hospital by means of a reference technique (DEXA), is a predictive factor for the occurrence of NI in the next 3 weeks.

The other risk factors for NI identified have often been cited in previous studies and have been demonstrated to be involved in NI, particularly in intensive care units (Harkness *et al.* 1990; Michel *et al.* 1991; Hanson *et al.* 1992; Cunnion *et al.* 1996; Hussain *et al.* 1996; Kampf *et al.* 1997; Wischnewski *et al.* 1998; Pittet *et al.* 1999; Klavs *et al.* 2003; Rothan-Tondeur *et al.* 2003; Gikas *et al.* 2004). It is clear that invasive devices are a risk factor for NI, as they account for four of the seven factors identified. As for invasive devices, the risk of NI associated with swallowing problems is probably due to the creation of an additional route of entry for the bacterium. In contrast, sarcopenia may increase the risk of NI by decreasing immunity.

These factors may also be linked in some way. For example, we could hypothesise that susceptibility to NI is restricted to malnourished patients because of their inability to eat, or to the very ill, who require more medical procedures. Multivariate analyses in a larger study could be used to address this issue. However, all these pathological conditions probably act in a synergistic manner, creating a vicious cycle of malnutrition–infection–use of invasive medical techniques. Paradoxically, assistance with feeding and the use of artificial parenteral nutrition via a gastric probe are obvious ways to combat sarcopenia. It therefore remains unclear whether independent risk factors can be distinguished.

In contrast, it would be interesting to determine the extent to which this vicious circle can be broken. The early withdrawal of medical devices is an established recommendation, as is the early treatment of infections. It is also recommended that

Table 2. Comparison of nutritional parameters, on admission, between the two groups of patients (nosocomial infection (NI) and non-NI group) identified at the end of the study

	Men				Women				Both sexes			
	NI group (*n* 13)		Non-NI group (*n* 22)		NI group (*n* 16)		Non-NI group (*n* 50)		NI group (*n* 29)		Non-NI group (*n* 72)	
	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD
Weight (kg)	66·7	12·8	71·2	17·3	55·2	12·8	53·3	11·2	60·4	13·9	58·8	15·6
BMI (kg/m^2)	22·7	3·9	23·8	4·8	24·8	6·9	24·6	5·0	23·9	5·8	24·3	4·9
C-reactive protein (mg/l)*	22·8		19·6		11·2		8·4		15·4		10·8	
Albumin (g/l)	29·1	7·4	30·1	3·8	28·6	7·4	31·5	5·1	28·8	7·3	31·1	4·7
Transthyretin (mg/l)	151·5	58·6	169·7	57·9	154·4	64·9	170·3	46·4	153·1	61·0	170·1	49·8
ASM /height^2 (kg/m^2)	6·9	1·5	7·1	1·0	6·7	1·5	6·9	1·0	6·8	1·5	6·9	1·0

NI, nosocomial infection; ASM, appendicular skeletal muscle mass.
* Expressed by geometric means owing to non-normal distribution.

carers be trained in the management of swallowing problems. These recommendations for good clinical practice have already been implemented. The present study, which aimed to identify the nutritional parameters most predictive of NI, was designed to make it possible to identify the patients most likely to benefit from early preventive nutritional care. PEM has been shown to decrease immunity (Lipschitz & Udupa, 1986; Chandra, 1992; Good & Lorenz, 1992; Mazari & Lesourd, 1998; Lesourd & Mazari, 1999; Cederholm *et al.* 2000). However, PEM is defined in many ways, the most widely used definition being based on weight loss. The other criteria used in clinical practice do not depend on repeated measures and are of three types: calorie intake, determination of serum albumin, transthyretin or leptin concentration, and diverse measures of body composition, including the calculation of BMI, the measurement of skin folds and of the brachial perimeter, bioelectrical impedance or DEXA (Lemonnier *et al.* 1991; Constans *et al.* 1992; Potter & Luxton, 1999; Kyle *et al.* 2001).

These methods are not entirely equivalent in terms of use and usefulness. Serum albumin and serum transthyretin concentrations are routinely determined in care of the elderly.

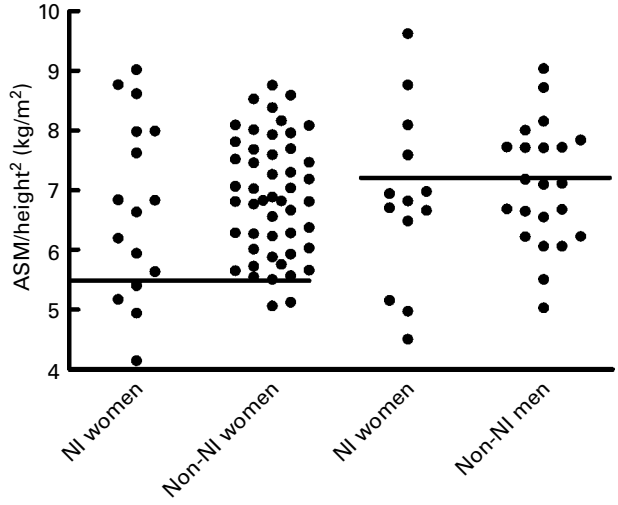

Fig. 2. Distribution of ASM/height^2 values on admission among patients subsequently presenting nosocomial infection (NI) or no such infection (non-NI) during their hospital stay. The horizontal lines represent the cut-off points defining sarcopenia. ASM, appendicular skeletal muscle mass.

These proteins are often considered to be markers of nutritional status, but their determination is actually not very specific and corresponds more closely to overall health status. The methods most frequently used to determine body composition in clinical practice, owing to their ease of use and low cost (BMI, bioelectrical impedance, measurements of skin folds and brachial perimeter), lack precision, accuracy and reproducibility (Erselcan *et al.*. 2000; Houtkooper *et al.* 2000; Fuller *et al.* 2001; Bedogni *et al.* 2003; Eckhardt *et al.* 2003; Sun *et al.* 2005).

DEXA is a method for determining body composition that presents all the characteristics of precision and reproducibility required in clinical practice (Baumgartner *et al.* 1995, 1998). This method is almost entirely innocuous (low doses of radiation, no injection of radioactive or nephrotoxic tracer), and the rapidity with which this method can be carried out makes it ideal for use in elderly patients (Mazess *et al.* 1990). DEXA can be used to generate independent measurements of different segments (limbs, head). Its principal limitations concern abnormalities in water metabolism (dehydration, oedema), because this technique cannot differentiate between water and muscle, and difficulties in interpreting the results in patients with prostheses. Reference values have been published only for men up to the age of 79 years (Newman *et al.* 2003) and for women up to the age of 95 years (Gillette-Guyonnet *et al.* 2003). No other method is as precise, reproducible, innocuous, easy and rapid to carry out as DEXA. The only real disadvantage of this method is its high cost.

This study provides important new scientific information. The use of a DEXA-based definition of sarcopenia made it possible to demonstrate a link between a low proportion of ASM on admission and the subsequent occurrence of NI. Indeed, the proportion of patients who were sarcopenic on admission was twice as high in the NI group as in the non-NI group. The diagnosis of sarcopenia by DEXA could be used to define a population at risk of NI, making it possible to target preventive action. The definition of sarcopenia used here was based on the ASM:height^2 ratio, which is considered the best parameter for evaluating skeletal muscle reserves (Melton *et al.* 2000; Tanko *et al.* 2002). However, the mean values for ASM:height^2 did not differ significantly between the two groups, with a β risk of only 5 %. The cause of the asymmetrical distribution that this implies requires further study. The distribution of ASM:height^2 according to sex

and its relationship to the occurrence of NI suggested that the presence of sarcopenia on admission may have greater positive predictive value for NI in men, whereas the absence of sarcopenia on admission may have greater negative predictive value for NI in women.

This study provides no evidence to support the existence of a relationship between weight or BMI and the risk of NI during the 3 weeks following these measures. This is not surprising, given that these methods of nutritional evaluation are clearly cruder than DEXA measurements. Albuminaemia and serum transthyretin concentration were found not to be associated with the risk of NI in this study, even if the currently accepted threshold values were used. This is clearly because the levels of these two proteins frequently decrease during episodes of inflammation and in malnutrition owing to hypercatabolism, as occurs after infection. The patients included in this study had just been admitted to hospital and had no signs of infection, and C-reactive protein concentration and body temperature did not differ significantly between the two groups. Determinations of albuminaemia, serum transthyretin concentration, C-reactive protein concentration and body temperature on admission are therefore not good early markers of the risk of NI.

It has been clearly demonstrated that interindividual variability increases with age. The monitoring of changes in nutritional (BMI, body weight, albuminaemia, prealbuminaemia) and inflammatory (C-reactive protein concentration, body temperature) parameters is therefore undoubtedly more sensitive than individual measurements made only once. However, this reasoning cannot really be applied clinically in the cases of interest because recent reference values for all the parameters considered are rarely available for elderly patients before their admission to hospital.

We did not assess protein and energy intake in this study, and it is possible that sarcopenia worsened in sarcopenic patients after admission, owing to lower levels of dietary intake in these patients than in non-sarcopenic patients. This problem is aggravated by the greater dietary protein needs of elderly than young people, with the consumption of what was assumed to be an adequate amount of protein often resulting in a loss of skeletal muscle (Sullivan *et al.* 1999; Campbell *et al.* 2001). The moderate mean level of malnutrition observed in our patients should not be allowed to conceal the high level of heterogeneity between subjects. For example, albuminaemia concentrations varied between 15·9 and 43·2 g/l. We cannot rule out the possibility that a similar study carried out on patients hospitalised or ill for a longer period, and therefore probably displaying a higher degree of malnutrition, would have given different results for PEM. However, the conclusions drawn from such a study might not have been applicable to patients from inclusion. We consider the period of 3 weeks separating the measurement of body composition and the end of the study to be pragmatic, in that it corresponds to the timescale of hospitalisation in acute care of the elderly wards over which nutritional interventions should be seen to be effective.

In conclusion, this study confirmed a number of previously identified risk factors for NI during the first 3 weeks of hospitalisation in a care of the elderly ward. Based on a precise and accurate measurement of body composition, we have shown that sarcopenia on admission to an acute care of the elderly unit, as measured by X-ray absorptiometry, was associated with a doubled risk of NI during the first 3 weeks of hospitalisation. Further studies are required to determine the magnitude of the risk associated with sarcopenia and its independence from the other identified risk factors. NI is also related to other, potentially confounding or 'mediating' factors, such as swallowing problems, invasive devices and low levels of autonomy by creating an additional route of entry for the bacterium, even without a reduced immune capacity resulting from the sarcopenia. However, the impact on the occurrence of NI of strengthened early nutritional and functional management of patients sarcopenic on admission should be evaluated.

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