

## Malnutrition is an independent factor associated with nosocomial infections

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The aim of the present prospective study was to determine if malnutrition, measured using a simple validated score, is an independent risk factor for nosocomial infections (NI) in non-selected hospital in-patients. Between 29 and 31 May 2001, a survey on the prevalence of NI was conducted on all 1637 in-patients (61 (SD 25) years old) in a French university hospital as part of a national survey. Actual and usual body weights were recorded in all in-patients, and serum albumin levels were measured on all blood samples taken during the week before the study. Nutritional status was evaluated by using the nutritional risk index (NRI). Albumin values were obtained in 1084 patients, and complete weight information was obtained in 911. Therefore, NRI was calculated in 630 patients (61 (SD 20) years old): 427 (67.8%) were malnourished. NI prevalence was 8.7%: 4.4% in non-malnourished patients, 7.6% in moderately malnourished patients and 14.6% in severely malnourished patients. In univariate analysis, the odds ratios for NI were 1.46 (95% CI 1.2, 2.1) in moderately malnourished patients and 4.98 (95% CI 4.6, 6.4) in severely malnourished patients. In multivariate analysis, age, immunodeficiency and NRI class influenced NI risk. Vascular and urinary catheters, and surgical intervention, were the extrinsic factors associated with NI, with odds ratios ranging from 2.0 (95% CI 1.8, 2.6) for vascular catheters to 10.8 (95% CI 8.8, 12.6) for association of the three factors. In conclusion, in non-selected hospitalized patients, malnutrition assessed with a simple and objective marker is an independent risk factor for NI. An early screening for malnutrition may therefore be helpful to reduce the high prevalence of NI.

**Nosocomial infections: Protein–energy malnutrition: Hospitals: Surgical wound infection: Urinary catheterization: Immunocompromised host**

There are approximately 2 million nosocomial infections (NI) per year in the USA, and 600 000 per year in France (Jarvis, 1996; Anonymous, 2000). Patients who develop NI are two to three times as likely to die, 60% more likely to spend time in an intensive care unit, and two to five times more likely to be readmitted to hospital (Kirkland *et al.* 1999) than those who do not. It has been estimated that 1% of all patients with an NI die as a direct result of the infection, and that NI contribute to the death of 2.7% of all patients admitted to hospital (Anonymous, 1992). Thus, NI could be responsible for 6–10% of all intra-hospital deaths (Garcia-Martin *et al.* 2001). The excess duration of hospitalization secondary to NI ranges from 1–4 d for urinary tract infections to 6.8–30.0 d for pneumonia (Jarvis, 1996).

NI represent a direct economic liability of US\$5–10 billion per year in the USA and US\$760 million per year in Europe (Wenzel, 1985; Worming, 1994). The estimated extra direct costs per infection range from US\$558–593 for each urinary tract infection to US\$4947 for each case of pneumonia. In countries with prospective payment

systems based on diagnosis-related groups, hospitals lose from US\$583 to US\$4886 for each NI (Jarvis, 1996). Programmes that reduce the incidence of NI can substantially decrease morbidity and mortality and reduce the economic burden for patients and hospitals.

For the last 20 years, health professionals have been alerted to a high prevalence of malnutrition among hospitalized patients ranging between 20 and 60% (McWhirter & Pennington, 1994; Naber *et al.* 1997b). Malnutrition is independently responsible for an increased rate of hospital morbidity including infections, pressure ulcers and delays in wound healing (Naber *et al.* 1997a,b); all these conditions can result in an increased length of stay and mortality (Robinson *et al.* 1987; Anker *et al.* 1997; McClave *et al.* 1992; Galanos *et al.* 1997). Nutrition and infection interact through different pathways, the most important being an impairment of non-specific and cell-mediated immunity (Scrimshaw & SanGiovanni, 1997). Several studies have reported infections (most of them supposedly NI) as a complication of malnutrition in selected populations (McClave *et al.* 1992; Rady *et al.* 1997; Llop

**Abbreviations:** NI, nosocomial infections; NRI, nutritional risk index.

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*et al.* 2001). However, in these studies fulfilment of NI definitions was not mentioned or assessed, and it is impossible to confirm whether these infections were acquired in the hospital setting; therefore, until now, whether malnutrition is an independent factor associated with NI in non-selected hospital in-patients remains unknown. The aim of this prospective study was, therefore, to assess the influence of malnutrition on the prevalence of NI in non-selected hospital in-patients.

### Subjects and methods

Between 21 May and 23 June 2001, a nationwide survey of the prevalence of NI was conducted in every hospital ward in France that agreed to participate when asked by the local Committee Against Nosocomial Infections (Comité de Lutte contre les Infections Nosocomiales). Every type of ward (acute-care, intermediate-care, long-stay) was included, except for day- or night-care and outpatient clinics. The prevalence of active NI (excluding those whose treatment had been completed by the time of the study) was determined by a team of trained hospital investigators who visited each hospitalized patient and reviewed his/her medical records with a referring physician and nurse from each ward. Medical history reviewed included immunodeficiency (HIV infection with CD4 cells <0.5 G/l, cancer with metastasis, haemopathy, immunosuppressive treatment including steroids, chemotherapy and radiation therapy), surgery, presence of a vascular or urinary catheter, and anti-infectious treatment. NI was defined as a well-documented infection absent on admission, and surgical-site infection was defined as an infection occurring in the 30 d following surgery (1 year for an implant or a prosthesis); the Centers for Disease Control and Prevention's definitions of NI were fulfilled in each case (Garner *et al.* 1988; Horan *et al.* 1992). In order to detect NI, investigators relied on the patient's records (high temperature, antibiotic prescription, bacteriology tests ordered), and interviewed patients, physicians and nurses. Only those NI with clinical and/or biological confirmation were considered. A 48–72 h follow-up was sometimes necessary to confirm or refute the diagnosis. Systematic screening for urinary tract infection (Multistix 9 SG reagent strip; Bayer Diagnostics, Puteaux, France) was performed in all patients who had a urinary catheter in place the day of the survey or during any of the previous 7 d; a urine culture was performed if the strip was positive, and the strip alone was not used in the diagnosis of NI.

The University Hospital of Nice is a referral hospital in south-east France. In this hospital, the Food and Nutrition Liaison Committee (Comité de Liaison Alimentation-Nutrition) and the Comité de Lutte contre les Infections Nosocomiales decided to add a nutritional survey to the NI prevalence survey (which was conducted over 2 d), with the systematic determination of the nutrition risk index (NRI) in all in-patients. The NRI (Buzby *et al.* 1988) was calculated as follows:

$$\text{NRI} = 1.519 \times \text{serum albumin (g/l)} + 41.7 \\ \times (\text{current/usual body weight}).$$

Patients with NRI >97.5 were considered as non-malnourished, those with NRI 83.5–97.5 moderately malnourished, and those with a NRI <83.5 severely malnourished. Serum albumin levels were systematically measured on all blood samples taken between 21 and 30 May (week preceding the survey), and determined colorimetrically using bromocresol green dye binding with a Hitachi 917 analyser (Roche Diagnostics, Meylan, France). Usual body weight was recorded and current body weight measured during the week before the survey or during the survey by one of twelve registered dietitians who were part of every team. All subjects gave their informed consent and the study was performed according to the Helsinki Declaration of 1975 as revised in 1983, after oral and written information was given to all patients; their privacy was protected by the Commission Nationale Informatique et Libertés.

### Statistical analysis

Values are expressed as means and standard deviations. Comparisons between populations were performed using Student's *t* tests and  $\chi^2$  tests. A search for factors related to NI was performed. Before implementation, variables considered for the analysis were carefully examined to determine those that were closely correlated in order to eliminate redundant ones. The following variables were studied: age, gender, immunodeficiency, NRI and its elements, surgical intervention, length of stay, type of stay, ward specialty, presence or absence of a vascular or urinary catheter and anti-infectious treatment. Logistic regressions were performed to analyse the impact of these variables on NI. Statistical significance was set at  $P < 0.05$ . Statistical analyses were performed using JMP software (SAS Institute Inc., Cary, NC, USA).

### Results

We studied 1637 patients (801 men, 836 women; mean age 61.2 (SD 24.6) years). Serum albumin was measured in 1084 patients (66.0%) and complete weight data was obtained in 911 patients (57.5%); actual body weight was measured in 1131 patients and usual body weight recorded in 1061. NRI was calculated in 630 patients (38.5%) (326 men, 304 women; mean age 61.4 (SD 19.8) years). Table 1 shows the characteristics of both the total population and the NRI population. The global prevalence of NI was 8.7%; it was 8.1% in the NRI population ( $P = 0.66$ ). The main sites of infection are represented on Fig. 1. Forty-two of the seventy patients with urinary tract infections had asymptomatic bacteriuria (thirty-six had a urinary catheter in place). Among the twenty-eight with a symptomatic urinary infection, fifteen had a catheter in place. The urinary catheter had been placed on the day of the survey in thirty-three of the fifty-one patients with a catheter-associated urinary tract infection. The main micro-organisms involved in total infections are represented on Fig. 2. Bacteria most frequently encountered were *Escherichia coli* (*n* 29), *Staphylococcus aureus* (*n* 28), Enterococci (*n* 11), *Pseudomonas aeruginosa* (*n* 10) and *Campylobacter* (*n* 9).

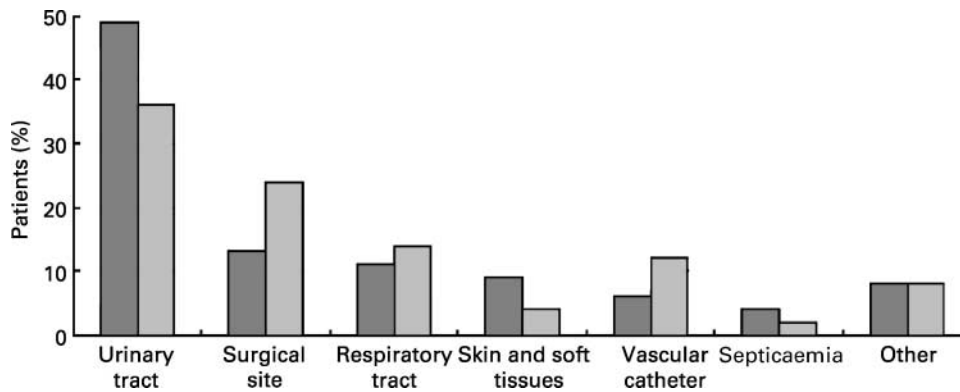
According to the NRI classification, 203 patients (32.2%) were not malnourished, 290 (46.0%) were

**Table 1.** Characteristics of all patients and patients in which the nutritional risk index was calculated\*

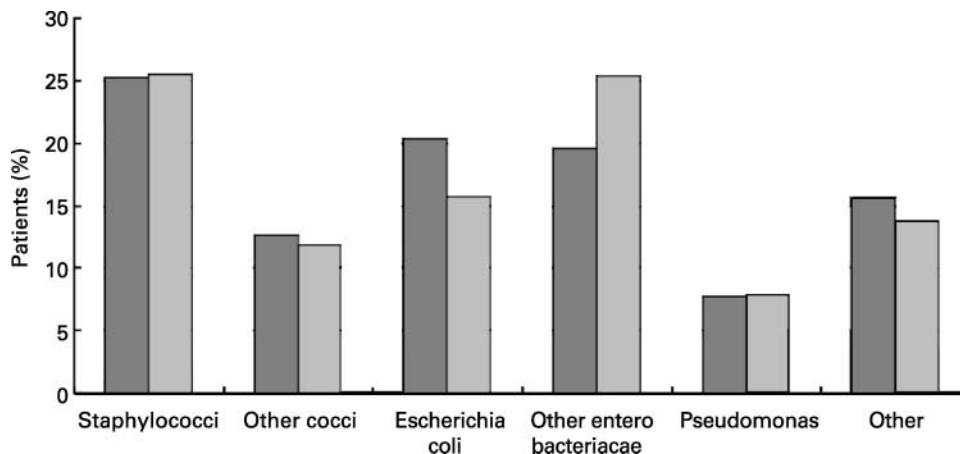
	All patients (n 1637)		NRI population (n 630)		Statistical significance of difference: P
	n	%	n	%	
Age (years) †	61.2	24.6	61.4	19.8	0.88
Gender-ratio (male (n): female (n))	0.96		1.07		0.23
Length of stay in acute-care wards (d) †	14	34	11	23	0.04
Ward specialty:					<0.0001
Medicine	828	50.6	393	62.4	
Surgery	379	23.2	153	24.2	
Geriatrics	281	17.1	54	8.6	
Intensive care units	77	4.7	17	2.7	
Other	72	4.4	13	2.1	
Type of stay:					<0.0001
Acute-care	1261	77.0	549	87.1	
Intermediate-care	235	14.4	78	12.4	
Long-stay	141	8.6	3	0.5	
Surgical intervention	377	23.0	144	22.8	0.72

\* For details of selection of patients, see p. 106.

† Mean values and standard deviations.



**Fig. 1.** Main nosocomial infection sites in all patients (n 1637) and in patients in whom the nutritional risk index (NRI) was calculated (n 630). ■, All patients; □, NRI population. For details of patients and procedures, see Table 1 and p. 106. Mean values were significantly different from those of all patients: \*P=0.50.



**Fig. 2.** Main bacteria responsible for nosocomial infections in all patients (n 1637) and in patients in whom the nutritional risk index (NRI) was calculated (n 630). ■, All patients; □, NRI population. For details of patients and procedures, see Table 1 and p. 106. Mean values for NRI group were not significantly different from those of all patients: P=0.99.

moderately malnourished and 137 (21.8%) were severely malnourished.

The prevalence of NI was 4.4% in non-malnourished patients, 7.6% in moderately malnourished patients and

14.6% in severely malnourished patients ( $\chi^2$  test,  $P=0.009$ ). In univariate analysis, the following patient-associated variables were found to be associated with NI: serum albumin levels ( $r^2$  0.04,  $P=0.04$ ), age ( $r^2$  0.06,

**Table 2.** Risk factors for nosocomial infection\*†

Patient-related factors			Procedure-related factors		
Variable	Odds ratio	95 % CI	Variable	Odds ratio	95 % CI
NRI			Type of stay		
≥97.5	1.00		Acute-care	1.00	
83.5–97.5	1.46	1.21, 2.11	Intermediate-care and long-stay	5.73	5.38, 6.08
<83.5	4.98	4.60, 6.40			
Age			Length of stay		
≤40 years	1.00		≤7 d	1.00	
>40 years	1.97	1.84, 2.10	>7 d	5.07	4.87, 5.27
Current weight			Surgical intervention		
≥50 kg	1.00		No	1.00	
<50 kg	10.40	9.50, 11.30	Yes	2.90	2.51, 3.29
Plasma albumin			Urinary catheter		
≥35 g/l	1.00		No	1.00	
<35 g/l	1.36	1.34, 1.38	Yes	9.00	8.87, 9.13
Immunodeficiency			Vascular catheter		
No	1.00		No	1.00	
Yes	1.80	1.45, 2.15	Yes	2.08	2.07, 2.09

NRI, nutritional risk index.

\*For details of patients and procedures, see Table 1 and p. 106.

†Univariate analysis by multiple logistic regression.

$P=0.05$ ), actual weight ( $r^2$  0.054,  $P=0.02$ ), immunodeficiency ( $r^2$  0.14,  $P=0.0007$ ) and NRI ( $r^2$  0.12,  $P=0.01$ ). The following procedure-associated variables were found to be associated with NI: length of hospital stay ( $r^2$  0.034,  $P=0.06$ ), type of stay ( $r^2$  0.065,  $P=0.04$ ), surgical intervention ( $r^2$  0.12,  $P=0.001$ ), presence of a vascular catheter ( $r^2$  0.16,  $P=0.0001$ ), presence of a urinary catheter ( $r^2$  0.39,  $P<0.0001$ ). Neither the type of ward (medical, surgical, geriatric, intensive care unit) nor the antibiotics received on the day of the survey influenced the risk of NI. Table 2 shows the odds ratios associated with each of these variables. In multivariate analysis, patient-associated variables significantly associated to the risk of NI included immunodeficiency ( $P=0.002$ ), age ( $P=0.01$ ) and NRI ( $P=0.03$ ); procedure-associated variables were surgical intervention ( $P=0.01$ ), presence of a vascular catheter ( $P=0.007$ ) and presence of a urinary catheter ( $P<0.0001$ ), with odds ratios ranging from 2.08 (95 % CI 1.82, 2.62) for vascular catheters to 10.80 (95 % CI 8.80, 12.60) for association of the three. The retrospective analysis of the length of stay was 11.1 (SD 34.8) d in non-malnourished patients, 17.5 (SD 37.4) d in moderately malnourished patients and 22.0 (SD 25.5) d in severely malnourished patients ( $\chi^2$  test,  $P=0.0034$ ).

## Discussion

The present prospective study shows a prevalence of NI of 8.7 % in an urban university hospital (approximately 2000 beds), with a marked relationship to the nutritional status. Malnutrition, as assessed by the NRI, was independently associated with a higher prevalence of NI.

Surveillance of NI has been widely accepted as a primary step toward prevention of NI (Haley, 1995). The gold standard is a prospective, on-site, continuous, hospital-wide surveillance. However, these incidence surveys require extensive resources. Therefore, prevalence studies, which are easier to perform and less expensive, are often

conducted to provide baseline information about the occurrence of NI and to help establish priorities for infection control. Most European countries, as well as the USA, Australia, Thailand and Mauritius, have organized prevalence studies (Gastmeier *et al.* 1998; Weinstein *et al.* 1999). An international prevalence study also has been conducted by the WHO (Mayon-White *et al.* 1988).

Many variables have been used to describe the nutritional status of hospitalized patients, including assessments of oral intake, body weight and loss of body weight, anthropometric data, hepatic secretory proteins and body composition analysis. However, even if these epidemiologically useful indicators correlate with morbidity and mortality (Mullen *et al.* 1979), no single measurement is of value in individual patients (Schneider & Hébuterne, 2000). Albumin is an integrative biological marker, which is associated with both body composition and the acute-phase response in patients. For this reason it is a very good cumulative variable of individual disease stage and activity, but usually not nutritional status (Klein, 1990), as it may be found in various other conditions (including hepatic and renal failure) and more generally in any situation when a systemic inflammatory response is involved, following injury, infection or inflammation (Rady *et al.* 1997; Llop *et al.* 2001; McMillan *et al.* 2001). Many studies have shown that albumin has strong prognostic power in numerous disease states, which makes it an ideal tool for stratifying patient groups. For example, hypoalbuminaemia alone has proved to be a valid negative prognostic factor, being associated with increased occurrences of NI, length of stay and mortality (Herrmann *et al.* 1992; McClave *et al.* 1992; Rady *et al.* 1997; Llop *et al.* 2001). Consequently, several clinical scores have been developed, including the NRI (Buzby *et al.* 1988). The NRI takes into account semi-starvation and the systemic inflammatory response, both relevant causes of hospital malnutrition. It is simple to calculate, inexpensive and reproducible. Furthermore, two studies



suggest that NRI is more accurate than the subjective global assessment in determining which patients are most at risk of contracting an infection (Naber *et al.* 1997b) and which patients will benefit the most from nutritional support (Anonymous, 1991).

The overall prevalence of NI in our present study is comparable with that found in other point-prevalence studies in teaching hospitals or medical centres with more than 500 beds (4.4–14.8%; Mayon-White *et al.* 1988; Weinstein *et al.* 1999; Anonymous, 2000). The particular strength of the present study is the in-depth analysis of possible intrinsic and extrinsic risk factors for NI.

Urinary tract, surgical sites and respiratory infections accounted for >70% of all infections, both in all patients and in the NRI population. The bacteria causing the infections, mainly staphylococci and gram-negative bacilli, were also comparable between the two populations. The high prevalence of urinary tract infections and the high-risk of NI in patients with a urinary catheter are well known (Weinstein *et al.* 1999). Moreover, the systematic screening for urinary tract infections in patients who had had a urinary catheter in place on the day of the survey, or in any of the 7 d before the survey, certainly enhanced the recognition (and therefore the prevalence) of urinary tract infections. Despite the very high odds ratio reported for urinary catheters, the other correlations found were significant, which is why we did not exclude urinary tract infections (which are one of the most common forms of NI) from the statistical analysis. However, this high odds ratio led us to separate patient-related variables from procedure-related variables in the multivariate analysis, as otherwise the former would have lost statistical significance.

There was no difference in age and gender between the population in which NRI was measured and the total hospital population. The prevalence and characteristics of NI were also similar in both populations, allowing us to apply the NRI group findings to the general population. However, NRI could only be calculated in three out of the 141 long-stay patients. There were several reasons: (1) lack of albumin values, since no blood sample was taken especially for the purpose of the present study (as this population with a long-term stay rarely has blood drawn, this explains the low number of albumin values obtained); (2) lack of knowledge of usual weight, as recalling usual weight can be difficult in demented or severely ill patients, who represent an important part of this population; (3) lack of current weight, since measuring weight on scales is impossible in bedridden patients without special devices that were absent from these facilities. We believe that the difference in ward specialty between the NRI population (more medical wards, less geriatrics) and the total population did not introduce an important bias, as accommodation is comparable in both types of wards, and the staff follow the same procedures.

Malnutrition was present in 68% of the patients: 46% were moderately malnourished and 22% were severely malnourished. Protein–energy malnutrition, or the possibility of developing it, has been reported to occur in 37–82% of patients in urban teaching hospitals (Tucker & Miguel, 1996), so our present results fall in the upper range. This

wide range may be explained by differences in the criteria used in assessing malnutrition and in the case mix of patients in the various hospital populations (Naber *et al.* 1997a). The prevalence of severe malnutrition in comparable studies ranges from 6% (Naber *et al.* 1997b) to 23.1% (Kyle *et al.* 2002) using the subjective global assessment, and from 8.4% (Anonymous, 1991) to 13% (Naber *et al.* 1997b) using the NRI. However, only one study is similar to ours in that non-selected patients admitted to every ward of a university hospital (Geneva, Switzerland) were enrolled; in that study, a prevalence of severe malnutrition of 23.1% was reported (Kyle *et al.* 2002). Our present study, like others (Edington *et al.* 2000; Thomas *et al.* 2002), found an increased length of stay in malnourished patients.

Analysis of factors associated with NI revealed several independent variables. Extrinsic factors associated with NI included surgery and the presence of vascular and/or urinary catheters. Association between these factors and NI has been shown (Setia *et al.* 1985; Trilla *et al.* 1991). Intrinsic factors included age and immunodeficiency (Setia *et al.* 1985; Trilla *et al.* 1991): immunodeficiency had the strongest statistical relationship with NI among patient-related variables, probably because, as with albumin, it is to a large extent a marker of disease stage and activity. Intrinsic factors also included malnutrition. A recent study of 4000 patients hospitalized in Brazil found the variables age >60 years, cancer, infection and length of hospital stay >15 d as independent risk factors for malnutrition (Waitzberg *et al.* 2001). However, the analysis makes it difficult to ascertain if infection favours malnutrition or if it is malnutrition that induces infection. The diagnoses and the severity of illness were not recorded in our patients, but strong evidence from the literature allows us to think that they probably did not affect the statistical link between malnutrition and the risk of NI (Sullivan & Walls, 1995), especially as our statistical model included diseases such as AIDS and metastatic cancer, and immuno-suppressive treatment.

As it both treats semi-starvation and provides metabolic support to patients who are experiencing a significant systemic inflammatory response, artificial nutrition reduces the complications (especially infectious) in severely malnourished patients (Anonymous, 1991); this is why screening for malnutrition is aimed at providing nutritional support in order to prevent co-morbidities. A study has shown that for each 2 d of earlier nutritional support there was a decline of 1 d in length of stay for the average patient (Tucker & Miguel, 1996). Unfortunately, references to nutritional status are present in less than half of the patients' hospital records (McWhirter & Pennington, 1994; Waitzberg *et al.* 2001) and untrained physicians fail to detect malnutrition (Roubenoff *et al.* 1987). As a result, nutritional status declines during the course of hospitalization (Weinsier *et al.* 1979; Gariballa, 2001). Health professionals need to be more aware of malnutrition and its consequences, and the presence of nutritional support teams will certainly help to increase awareness among professionals, with the ultimate aim of reducing the prevalence and consequences of hospital malnutrition (Hassell *et al.* 1994). The strong statistical relationship between

malnutrition and NI leads us to hypothesize that addressing hospital malnutrition will lead to a decrease in the number of NI, as implementation of malnutrition screening and treatment at hospital scale has been showed to reduce length of stay, cost of care and severe disease complications (Brugler *et al.* 1999). Therefore, this calls for intervention studies. Finally, knowing the consequences of malnutrition and not looking for it may have medico-legal consequences.

In conclusion, NI are one of the many consequences of malnutrition in a hospital setting. Early screening for malnutrition may therefore be helpful to reduce the high prevalence of NI.

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