Research article

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Total parenteral nutrition is associated with worse hospital outcomes among elderly diabetic patients: a propensity score matched analysis on discharge records

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Abstract

Background. Recent trials and reviews have raised question about the safety of total parenteral nutrition (TPN), due to the increased rate of TPN related complications. Diabetic patients are vulnerable to hyperglycaemia, and poor studies have investigated hospital outcomes of diabetic patients requiring TPN. The aim of this study was to evaluate the association of in-hospital mortality, prolonged length of stay and transfer to long-term care facilities among diabetic patients with TPN.

Methods. The study considered all hospital admissions of diabetic patients over 65 years of age performed between 2006 and 2015 in Abruzzo Region, Italy. To compare the outcomes of TPN and non-TPN patients, a propensity score matching procedure was performed.

Results. A total of 140,556 admissions were analyzed. After matching, 1947 patients were included into the analyses: 649 patients with TPN and 1298 controls. TPN was significantly associated to in-hospital mortality (OR=7.15; 95%CI 5.54-9.22), prolonged LOS (OR=2.78; 95%CI 2.28-3.38) and transfer to LTCF (OR=2.16; 95%CI 1.64-2.85).

Discussion. TPN is associated with poor outcomes among elderly diabetic patients in the Italian setting. Being aware of the risk factors among diabetic patients with TPN can be used to anticipate the patients' needs during the admission and the immediate post-discharge period.

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Key word: *diabetes, parenteral nutrition, outcomes, HDR, epidemiology*

Introduction

Malnutrition is highly prevalent in hospitalized patients and it is associated with increased risk of hospital complications, higher mortality rate, and higher resource utilization (1). Parenteral nutrition (PN) is the provision of macronutrients, micronutrients, electrolytes and fluid infused as an intravenous solution and provides a method for people to receive nutrients when they are unable to achieve adequate nutritional intake (2). In malnourished patients, parenteral nutrition can improve nutritional and immunologic status (3,4,5).

However, recent randomized trials and systematic reviews have raised question about its safety, due to the increased rate of total parenteral nutrition (TPN) related complications (4,6).

In particular, the increased risk of complications and mortality can be related to the onset of hyperglycaemia, particularly in critically ill patients (7–10).

Several studies have demonstrated a relation between hyperglycaemia and mortality for stroke(11), myocardial infarction (12), and increased infection rates, respectively (13,14).

The mechanism underlying the negative effect of hyperglycaemia are not fully understood, but may be related to inflammation and to alteration of immune system (15,16).

A group of patients who should be particularly vulnerable to hyperglycaemia are diabetic patients that frequently face off a glucose impairment due to an acute event. Complications occurring during a hospitalization may lead to higher in-hospital mortality and prolonged length of stay, particularly for infectious complications (17).

In addition, patients with diabetes and TPN need particular transitional care after discharge, frequently requiring transfer to long-term care facilities (18,19).

Poor studies investigated the hospital outcomes of diabetic patients requiring TPN in the Italian setting.

The aim of this study was to evaluate the association of in-hospital mortality, prolonged length of stay (LOS) and transfer to long-term care facilities with TPN among diabetic patients in an Italian region. As a secondary outcome, the occurrence of complications during the hospital stay was investigated.

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Methods

The study considered all hospital admissions of diabetic patients over 65 years of age performed between 1st January 2006 and 30th December 2015 in Abruzzo, Italy. Abruzzo is a region of central Italy, counting over 1.2 million inhabitants and 29 hospitals, comprising 18 public hospitals and 11 private clinics. Data were collected from all hospital discharge records (HDR), which include information on the patient's demographic characteristics, a Diagnosis Related Group code (DRG, grouped in 25 Major Diagnostic Category - MDC) used to classify the admission, and up to 6 diagnoses and 5 procedures performed during the hospitalization, coded as per the International Classification of Disease, 9th Revision, Clinical Modification (ICD-9-CM). Patients with Codes 250.xx recorded as the principal or one of the secondary diagnoses were taken into account. TPN was identified by the code 99.15, reported in the procedure (performed). Admissions lasting over 15 days were considered as 'prolonged LOS'. This value represented the upper quartile of the overall population's LOS distribution. The secondary outcomes considered were glycaemic impairment, hyperosmolar state and occurring of acute myocardial infarction (AMI), stroke or any infectious disease.

Statistical analysis

Quantitative variables were summarized as mean and standard deviation (SD) or median and interquartile range (IQR) according to their distribution. Qualitative variables were summarized as frequency and percentage. To compare the outcomes of TPN and non-TPN patients, a propensity score matching procedure was performed using a multivariable logistic model with a 8:1 greedy matching algorithm with no replacement. All baseline variables included in the matching model are listed in Table 1. In particular, all the items in Elixhauser comorbidity index (20), age, gender and myocardial infarction were taken into consideration. The adequacy of covariate balance in the matched sample was assessed via standardised mean differences between the two groups, with differences of less than 10% indicating a good balance (21). The matching ratio between cases and controls was 1:2. Patients, for whom no match was found, were discarded from the matched analyses. Odds ratios with their 95% confidence intervals (95%CI) were computed using logistic regression models, adjusted for propensity score as covariate. 2-tailed P values less than 0.05 were considered significant. The statistical analysis was performed using IBM SPSS Statistics v23.0 (SPSS Inc. Chicago, Illinois, USA).

Compliance with Ethical Standards

The study was conducted in conformity with the regulations on data management of the Regional Health Authority of Abruzzo and with the Italian Law on privacy (Art. 20-21 DL 196/2003) published on the Official Journal n. 190 of August 14, 2004. Data were encrypted prior to the analysis at the regional statistical office, where each patient was assigned a unique identifier. This identifier eliminates the possibility to trace the patient's identity. According to the Italian laws, no written informed consent is required when the data are anonymous. The usage of this database was approve by the Department of Health and Welfare of Abruzzo Region.

Fundings

Funding information is not applicable.

Conflict of interest

The authors declare that they have no conflict of interest.

Results

A total of 140,556 admissions of diabetic patients over 65 years of age were performed in Abruzzo region during the study period; 653 admissions (0.5%) required TPN. After matching, 1947 patients were included into the analysis: 649 patients with TPN and 1298 controls (Fig. 1). Table 1 shows the baseline patient's characteristics. In the unmatched study population, TPN patients were older and had fewer preoperative comorbidities. In comparison with the unmatched population, patients with TPN included in the matched population had the same age (mean age 80.19 years for the matched population vs. 80.18 years for the unmatched population), while the patients without TPN included in the matched population were older (mean age: 80.29 years in the matched population vs. 77.66 years in the unmatched population). After matching, there were no differences in the baseline characteristics between the two groups (Table 1), with standardized mean differences all below 0.10. In the matched population, both study groups were mainly admitted to hospital for acute heart failure, as showed in Table 2. Other frequent causes of admission were lung diseases and diabetes. Table 3 reports the analysis of the outcomes relating to the matched study groups. In the matched population, TPN was significantly associated to in-hospital mortality (OR=7.15; 95%CI 5.54-9.22), prolonged LOS (OR=2.78; 95%CI 2.28-3.38) and transfer to LTCF (OR=2.16; 95%CI 1.64-2.85). In addition, TPN was associated to a higher risk of glycaemic decompensation (OR=1.49; 95%IC 1.18-1.87). No association was found for AMI, stroke and infectious diseases. Only a sub-analysis that investigated the likelihood to get pneumonia during hospitalization resulted significant (OR=2.05; 95%IC 1.43-2.93).

Discussion

The analysis of a large cohort of Italian diabetic patients older than 65 years evidenced that TPN, after matching for baseline characteristics, reported poor in-hospital outcomes comparing with patients without TPN. In particular, TPN patients had a higher risk for in-hospital mortality, confirming the result of Oliveira et al (7) that conducted a multicenter study on in-hospital mortality in a cohort of non-critically ill Spanish patients that underwent TPN. The main reason of these findings was probably due to the increased serum glucose level during the infusion of TPN. It is widely confirmed by many other studies that investigated both intensive care unit patients (6,8,10,22-24)and non-critical patients (25). In the past, hyperglycaemia was believed to be an adaptive response, but nowadays it is a demonstrated

Table 1. Patients' baseline characteristic before and after matching procedure

	Unmatched		Matched		
	TPN+ (n=653) (n%)	**TPN- (n=139,903) (n%)**	**TPN+(n=649) (n%)**	**TPN- (n=1298) (n%)**	**Standardized mean difference**
Age mean±SD	80.18±7.61	77.66±7.04	80.19±7.61	80.29±7.39	-0.017
Female gender	334(51.1)	69,211(49.5)	332(51.2)	654(50.7)	0.009
Myocardal infarction	27(4.1)	9184(6.6)	27(4.2)	50(3.9)	0.015
Congestive hearth Failure	71(10.9)	21,994(15.7)	71(10.9)	144(11.0)	-0.005
Cardiac arhytmias	62(9.5)	17,629(12.6)	62(9.6)	127(9.8)	-0.008
Valvular diseas	9(1.4)	6,801(4.9)	9(1.4)	15(1.2)	0.020
Pulmonary circulation disorders	9(1.4)	1,096(0.8)	9(1.4)	22(1.6)	-0.026
Periferal vascular disease	20(3.1)	9,259(6.6)	20(3.1)	36(2.8)	0.018
Non complicated Hypertension	115(17.6)	41,559(29.7)	115(17.7)	218(16.9)	0.024
Complicated Hypertension	92(14.1)	14,526(10.4)	91(14.0)	190(14.6)	-0.018
Paralysis	2(0.3)	297(0.2)	2(0.3)	1(0.1)	0.042
Neurodegenerative disordes	18(2.8)	2,165(1.5)	18(2.8)	39(3.0)	-0.014
Chronic pulmonary disease	85(13.0)	17,255(12.3)	85(13.1)	197(15.2)	-0.064
Hypothyroidism	3(0.5)	1,830(1.3)	3(0.5)	10(0.7)	-0.046
Renal failure	63(9.6)	14,955(10.7)	63(9.7)	134(10.3)	-0.021
Liver disease	24(3.7)	6,684(4.8)	24(3.7)	48(3.7)	0.001
Peptic ulcer	1(0.2)	247(0.2)	1(0.2)	4(0.3)	-0.039
HIV/AIDS	-	68(0.0)	-	-	0
Solid tumor without metastasis	154(23.6)	11,102(7.9)	150(23.1)	277(21.3)	0.040
Metastatic cancer	69(10.6)	2,653(1.9)	67(10.3)	105(8.1)	0.073
Lymphoma	3(0.5)	822(0.6)	3(0.5)	7(0.6)	-0.011
Reumathoid arthritis/collagen vascular diseases	6(0.9)	1,362(1.0)	6(0.9)	14(1.1)	-0.016
Coagulopathy	4(0.6)	524(0.4)	4(0.6)	10(0.8)	-0.020
Obesity	14(2.1)	3174(2.3)	14(2.2)	27(2.1)	0.005
Weight loss	41(6.3)	348(0.2)	37(5.7)	59(4.5)	0.022
Electrolite disorders	38(5.8)0	2,392(1.7)	37(5.7)	67(5.2)	0.10
Blood loss anemia	14(2.1)	1,351(1.0)	13(2.0)	29(2.2)	-0.021
Deficiency anemia	22(3.4)	3,707(2.6)	22(3.4)	35(2.7)	0.038
Alcohol abuse	-	73(0.1)	-	-	0
Drug abuse	-	19(0.0)	-	-	0
Psychosis	5(0.8)	1,066(0.8)	5(0.8)	5(0.4	0.044
Depression	1(0.2)	1,450(1.0)	1(0.2)	2(0.2)	0.001
Complicated diabetes	86(13.2)	24,952(17.8)	86(13.3)	184(14.1)	-0.027

Abbreviations: TPN=Total parenteral nutrition.

Table 2. Most frequent causes of admission among studied population, with relatives ICD-9-CM codes

NPT- (n=1298)	n(%)	NPT+ (n=649)	n(%)
Acute heart failure (428.xx)	116(8.9)	Acute heart failure (428.xx)	72(11.1)
Other lung diseases (518.xx)	60(4.6)	Diabetes (250.xx)	39(6.0)
Diabetes (250.xx)	47(3.6)	Other lung diseases (518.xx)	25(3.9)
Atherosclerosis (440.xx)	46(3.6)	Stroke (434.xx)	17(2.6)
Arythmias (427.xx)	43(3.3)	Hypertensive heart diseases (402.xx)	16(2.5)
Myocardial infarction (410.xx)	40(3.1)	Myocardial infarction (410.xx)	16(2.5)
COPD (491.xx)	35(2.7)	Arythmias (427.xx)	14(2.2)
Chronic heart diseases (414.xx)	32(2.5)	Fracture of neck of femur (820.xx)	14(2.2)
Others	797(66.9)	Others	425(66.5)

Abbreviations: TPN=Total parenteral nutrition; COPD=Chronic Obstructive Pulmonary Disease.

Table 3. Outcomes in Matched Population

	TPN+(n%)	TPN-(n%)	Odds Ratio[+]	95%CI	p-value
In-hospital mortality	250(38.5)	104(8.0)	7.15	(5.54-9.22)	<0.001
Prolonged LOS	329(50.7)	348(26.8)	2.78	(2.28-3.38)	<0.001
Transfer to LTCF	116(17.9)	118(9.1)	2.16	(1.64-2.85)	<0.001
Glycaemic decompensation	160(24.7)	232(17.9)	1.49	(1.18-1.87)	0.001
Hyperosmolar state	8(1.2)	19(0.5)	0.91	(0.37-1.91)	0.672
Myocardial infarction	61(9.4)	123(9.5)	1.01	(0.44-1.61)	0.785
Stroke	128(19.7)	213(16.4)	1.25	(0.98-1.59)	0.076
Any infectious diseases	11(1.7)	16(1.2)	1.36	(0.63-2.95)	0.437

All models were adjusted for propensity score
[+] Odds ratios of TPN+ over TPN-
Abbreviations: TPN=Total parenteral nutrition; CI=Confidence interval; LOS=Length of stay; LTCF=Long term care facilities

risk factor for increased mortality and morbidity in various medical conditions (8,26–29).

Diabetic population can be at a higher risk for in-hospital death compared to non-diabetic patients, in particular if the glycaemic control is poor, contributing to an added risk of worse outcomes (22).

The higher risk of glycaemic decompensation among TPN patients strongly confirms this finding. Hyperglycaemia could favour the occurrence of infectious complications, hampering early discharge and prolonging the stay of patients (7,30).

In this study, the incidence of any infectious disease was not different between the groups, probably due to the low incidence of the events. Only pneumonia was significantly associated to TPN. No significant differences were also found for other in-hospital complications investigated.

Beyond eventual complications occurred during hospitalization, TPN patients are frequently discharged to LTCF. This can be explained by the need of higher level of care for TPN patients: home is frequently not the proper environment for managing TPN, and home-care services are frequently not enough for this aim. Recently, increased attention has been given to different aspects of diabetes care with regard to discharge planning: diabetic patients frequently face off hospital readmission and short-term complications (31,32), so it is important to identify the risk factors for readmission and complications in patients with diabetes, as for patients with other comorbidities (33,34).

In addition, the specific out-hospital necessities of diabetic patients treated with TPN cause added costs and higher resources consumption for public health (18,19).

Strengths and limitations

The major strength of our study is represented by the large number of patients evaluated, making the study results very robust. Propensity score matching is also a robust methodology to limit possible confounders, as reported in previous studies (35). The study also has limitations. First, the identification of diagnosis is based on ICD-9-CM codes that do not take into account the severity of the conditions. Second, the use of administrative data may be limited by the reliability of certain types of information such as drugs therapy and clinical information. Finally, the true prevalence of some comorbid conditions could be underestimated, due to underreporting of their codes in the hospital discharge registry.

Conclusions

In conclusion, being aware of the risk factors in treating diabetic patients with TPN can/may avoid poor outcomes. It can also anticipate the patients' needs during the admission and the immediate post-discharge period. Moreover, it can help develop a specific care transition model, in order to improve the quality of care, develop a proper discharge planning and save resources.

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