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Effect on Whole-body Protein Synthesis after Institution of Intravenous Nutrition in Cancer and Non-cancer Patients who Lose Weight

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Cancer and non-cancer patients received total parenteral nutrition (TPN) corresponding to either 120% or 200% non-protein energy resting energy expenditure. Whole-body tyrosine flux and leg exchange of various metabolites were measured in the fasted and fed state. Feeding with the moderate TPN rate did not stimulate whole-body protein synthesis in either group, but the high rate did. Both TPN rates switched an efflux of branched-chain aminoacids from the leg to an uptake in both groups, but this did not apply to tyrosine or phenylalanine. Only the high TPN rate stimulated glucose uptake across the leg in both groups. The leg exchanges of lactate, glycerol and free fatty acids were not significantly influenced by moderate or high TPN rates in either group, although changes in arterial concentrations indicated significant exchanges in compartments other than leg tissues. Thus standard TPN is insufficient to stimulate overall protein synthesis in both malnourished cancer and non-cancer patients, which may explain why previous studies have demonstrated insignificant functional effects with nutritional support to cancer patients.
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INTRODUCTION

THERE IS scarce information about whether malnourished cancer patients use nutrients similarly to non-cancer patients with an identical degree of malnutrition. We have reported that undernourished cancer patients have normal whole-body capacity to oxidise non-protein energy after intravenous nutrition [1]. In our studies with enteral nutrition, we also found that whole-body energy balance and the use of non-protein energy were similar in undernourished cancer and non-cancer patients [2]. However, simultaneous studies on aminoacid flux across the leg indicated that a negative aminoacid balance occurred across the leg in cancer patients during nutrition, which suggests an insufficient restimulation of protein synthesis in response to nasogastric feeding [3]. If this finding indicates a general inability to use aminoacids for restoration of lean tissues in malnourished cancer patients, it is not surprising that most studies have reported insignificant effects on outcome by giving nutrition to cachexic cancer patients [4, 5]. We have since found that continuous home parenteral nutrition for 3 months in young men on chemotherapy for testicular carcinoma led to deposition of body fat and maintenance of body weight, but the nutritional intervention did not prevent the loss of lean tissues (A.H.C. Drott, B. Unsgaard, J. Tölli, U. Körner, B. Arfvidsson and K.L.). The insufficient effect by intravenous nutrition was assessed by repeated measurements of whole-body nitrogen by neutron activation. Thus, these findings may infer that standard intravenous nutrition was actually not effective to the extent that we expect it to be, at least when cancer patients receive drug treatment. Therefore, we aimed to establish whether standard intravenous nutrition effectively stimulates protein synthesis in malnourished cancer patients without previous drug or radiation treatment.

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PATIENTS AND METHODS

Patients

28 patients—11 women and 17 men—treated in our department were included. 12 of the patients had malignant disease; the other 16 had non-malignant disease and served as controls. None of the patients had received any cancer treatment before the study. All patients had normal liver function tests (bilirubin, alkaline phosphatases, aspartate aminotransferase, alanine aminotransferase) and normal serum creatinine. The diagnoses in the cancer group were: colonic carcinoma (n = 3), oesophageal carcinoma (1), leiomyosarcoma (1), pulmonary sarcoma (1), kidney carcinoma (1), rhabdomyosarcoma (1), adenocarcinoma (1), gastric carcinoma (1), malignant lymphoma (1) and malignant melanoma (1). The diagnoses in the control group were: gastric ulcer (3), duodenal ulcer (1), arterial insufficiency (3), oesophagitis (2), aortic aneurysm (2), chronic pancreatitis (1), aortic stenosis (1), cholecystolithiasis (1), colonic diverticulitis (1) and 1 patient admitted for abdominal pain probably due to abdominal angina. The nutritional state of the patients is presented in Table 1. Both groups had a weight index around 0.87 and were judged on clinical grounds as potential candidates for nutritional support. All patients ate a standard hospital diet (48% carbohydrate, 34% fat and 18% protein) at their own choice before the study.

The design was that two categories within each group should receive different nutrition regimens (moderate and high rate of total parenteral nutrition [TPN]). It was planned that each group should contain about 7 patients. The patients were thus randomised (envelope technique) to receive non-protein calories corresponding to either 120% or 200% of measured resting energy expenditure (REE) with 0.2 g and 0.33 g nitrogen per kg body weight, respectively.

Nutritional status

AMC and TSF were measured as described [6]. Serum albumin was analysed by the bromocresol green method [7]. TBK was measured in a whole-body counter [8]. PREE was calculated according to the Harris and Benedict formula [9]. Energy expenditure was measured by indirect calorimetry [10].

Whole-body protein kinetics

The patients were studied at rest in bed. Tyrosine kinetics was measured day 1 in the fasted state after an overnight fast and in the fed state during TPN infusion on day 2. After infusions and measurements of protein kinetics on day 1, patients were allowed to eat and drink freely until 2000 h, after which they were allowed to drink water only. The second measurement of protein kinetics was done the next morning after a 12 h fast. The TPN solution was now infused with the labelled aminoacid, [^{14}C]tyrosine [11].

During the fasted and fed states (days 1 and 2, respectively) whole-body protein kinetics was measured at steady-state conditions after a primed constant infusion of L-[U-^{14}C] tyrosine (22.2 kBq/kg) as described [12]. The experimental design was based on the times that we previously found necessary to obtain steady-state and isotopic plateau levels with and without intravenous infusions [11–14]. Thus, on day 1, [^{14}C]tyrosine was administered intravenously in 500 ml normal saline with a monoexponentially primed infusion followed by a constant infusion (80 ml/h, about 185 kBq) during 6 h in which an infusion pump (IVAC, Stockholm, was used [13]. The same pump was used for all isotopic infusions. Radial artery blood samples were drawn before infusions and at 4, 5 and 6 h after the start of infusion for measurement of the specific radioactivity in plasma tyrosine, which confirmed plateau values (within 8% variation) in agreement with our previous experiments [12, 14]. The mean specific radioactivity of plasma tyrosine was calculated from the samples taken at these times. Briefly, plasma samples were immediately precipitated with 10% trichloroacetic acid. Tyrosine was extracted and enzymatically converted to tyramine [12] and analysed fluorometrically [15]. The radioactivity was measured in a liquid scintillation counter. Specific radioactivity in expired carbon dioxide and the oxidation rate of tyrosine were measured during the last 30 min of [^{14}C]tyrosine infusion in a ventilated hood system [12]. Whole-body oxygen consumption and carbon dioxide production were also measured during the last 30 min of the infusion periods. Energy expenditure was calculated from measurements of respiratory gas exchanges [16].

On day 2, before the intravenous nutrition infusion was given, the resting oxygen consumption and carbon dioxide production were measured over 30 min. The residual $^{14}CO_2$ in expired gases was quantified and accounted for as blank values in subsequent calculations of tyrosine oxidation [13]. Zero-time blood samples were also taken to confirm that no residual radioactivity could be detected in free plasma tyrosine. The isotope was added to the aminoacid solution (29.6 kBq/kg) and was infused for 6 h, as on day 1 with the monoexponentially primed constant infusion. Blood samples for measurement of the mean specific radioactivity in plasma tyrosine were taken at 4, 5 and 6 h. Oxygen consumption, carbon dioxide production and tyrosine oxidation were measured again during the last 30 min of the [^{14}C]tyrosine infusion.

Calculation of tyrosine flux

Whole-body tyrosine flux, oxidation and tyrosine incorporation into proteins were calculated according to James *et al.* [17]. The mass fraction of tyrosine in protein was assumed to be 3%. Protein synthesis was calculated from the difference between whole-body tyrosine flux and oxidation of tyrosine. The limitation of this method has been discussed by Waterlow *et al.* [18]. Protein degradation was not estimated, since the contribution of tyrosine synthesis from phenylalanine is not measured by this kinetic model [18].

Intravenous nutrition

Measurements of REE on day 1 were used to calculate the individual nutritional need in each patient for TPN on day 2. 6 of the cancer patients and 7 of the controls were randomised to receive non-protein energy to a level corresponding to 120% of their REE with 0.2 g nitrogen per kg. The other 6 cancer patients and 9 controls received non-protein energy corresponding to 200% of their REE with 0.33 g nitrogen per kg. Half of the non-protein calories were given as a 30% D-glucose solution, the other half as a fat emulsion (Intralipid 20%). Nitrogen was

Table 1. *Nutritional status of the patients before treatment: mean (S.E.)*

	Cancer		Control	
	120%	200%	120%	200%
Age (yr)	68.0 (4.7)	69.3 (5.0)	67.3 (3.2)	69.0 (3.4)
Height (cm)	173.7 (4.3)	169.8 (3.3)	173.0 (2.0)	169.2 (2.9)
Weight (kg)	68.7 (3.9)	58.0 (1.9)	62.4 (2.7)	65.3 (4.5)
Weight reduction (%)	10.2 (2.6)	17.0 (4.0)	10.0 (2.7)	5.6 (2.9)
TSF (mm)	11.4 (2.1)	6.7 (1.1)*	8.4 (1.1)	12.7 (2.1)
AMC (cm)	22.2 (1.0)	20.9 (1.0)	23.3 (0.9)	23.3 (1.3)
TBK (mmol)	2860 (124)	2511 (169)	2847 (163)	2871 (295)
TBK index (%)	0.92 (0.04)	0.89 (0.08)	0.92 (0.05)	0.98 (0.04)
Plasma albumin (g/l)	29.8 (1.7)	27.9 (1.3)	31.2 (1.6)	34.7 (1.4)
PREE (kcal/day)	1363 (105)	1211 (28)	1321 (50)	1328 (83)

*Significantly different by ANOVA, $P < 0.05$.

TSF = triceps skinfold, AMC = arm muscle circumference, TBK = total body potassium and PREE = predicted resting energy expenditure.

Table 2. Energy expenditure and respiratory quotient in fasted and fed state

	Cancer		Control	
	120%	200%	120%	200%
REE (kcal/day)				
Fasted	1311 (105)	1296 (134)	1129 (78)	1095 (56)*
TPN	1361 (135)	1424 (160)†	1148 (92)	1274 (67)†
RQ				
Fasted	0.78 (0.01)	0.77 (0.01)	0.77 (0.04)*	0.79 (0.01)
TPN	0.78 (0.03)	0.85 (0.01)†	0.82 (0.01)†	0.84 (0.01)†

*Significantly different by ANOVA, $P < 0.05$.
†$P < 0.05$, fasting vs. TPN.

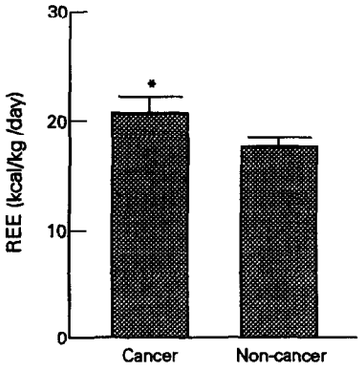

Fig. 1. Mean (S.E.) resting energy expenditure in fasted state in all cancer patients vs. non-cancer patients. Significant difference between groups, $P < 0.05$.

supplied as crystalline aminoacids (Vamin 14*, Kabi Nutrition AB, Sweden) containing tyrosine 0.17 g/l. Vitamins, minerals and trace elements were given according to routine recommendations. All solutions were infused simultaneously via a central venous catheter.

Substrate exchange across the leg

Substrate exchanges across the leg were measured after catheterisation of the radial artery and femoral vein with blood sampling simultaneously 6 h after start of the infusions at steady state. Leg blood flow was measured by a strain gauge plethysmograph [19]. Aminoacids were analysed by high-performance liquid chromatography [20]. Plasma samples were analysed for glucose and glycerol with kits from Boehringer Mannheim. Free fatty acids (FFA) were analysed by a colorimetric test (NEFA, Wako, Japan). All measurements were done during fasting (day 1) and TPN infusion (day 2). The leg exchange of aminoacids and substrates was calculated as the arteriovenous difference multiplied by the leg blood flow [2, 3].

Statistics

Comparison of the patient groups in the fasted and fed state was by a two-factor analysis of variance factorial (ANOVA) with a 95% CI. This comparison tested whether the various subgroups belonged to the same population or not. A *post hoc* test was used to test significance among subgroups. Comparisons within groups before and during TPN were tested by *t*-test for paired observations. $P < 0.05$ was considered significant.

*Composition of the aminoacid solution, Vamin 14 (g/l): glycine 5.9; aspartic acid 2.5; glutamic acid 4.2; alanine 12.0; arginine 8.4; cysteine/cystine 0.42; histidine 5.1; isoleucine 4.2; leucine 5.9; lysine 6.8; methionine 4.2; phenylalanine 5.9; proline 5.1; serine 3.4; threonine 4.2; tryptophan 1.4; tyrosine 0.17; valine 5.5.

RESULTS

56 infusions and 84 measurements of respiratory gas exchange were done in the 28 patients who were randomised into four groups with reasonably similar age and nutritional status. However, cancer patients receiving TPN infusions corresponding to 200% of their REE and 0.33 g nitrogen per kg had a significantly lower TSF (Table 1). Control patients (200%) had a significantly lower REE at fast compared with the other groups. Control patients (120%) had a significantly lower RQ (Table 2).

Energy expenditure

Cancer patients had a significantly higher resting energy expenditure in the fasted state compared with controls (Fig. 1). Energy expenditure was not affected by the low rate of TPN (120%) but was significantly increased by the high rate (200%)

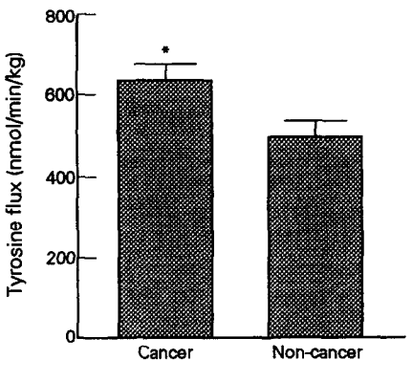

Fig. 2. Whole-body tyrosine flux in fasted state in all cancer patients vs. non-cancer patients. Significant difference between groups, $P < 0.01$.

Table 3. Whole-body tyrosine kinetics in fasted and fed state

	Cancer		Control	
	120%	200%	120%	200%
Tyrosine flux (nmol/min/kg)				
Fasted	542 (44)	721 (39)*	488 (61)	488 (31)
TPN	610 (60)	882 (77)†	475 (60)	625 (34)†
Tyrosine oxidation (nmol/min/kg)				
Fasted	29 (3)	45 (4)	29 (6)	32 (4)
TPN	50 (6)†	73 (3)†	37 (6)	61 (7)†
Tyrosine incorporation into protein (nmol/min/kg)				
Fasted	514 (41)	676 (39)*	459 (57)	456 (29)
TPN	560 (54)	809 (76)†	438 (55)	563 (28)†

*Significantly different by ANOVA, $P < 0.05$.
†$P < 0.05$, fasting vs. TPN.

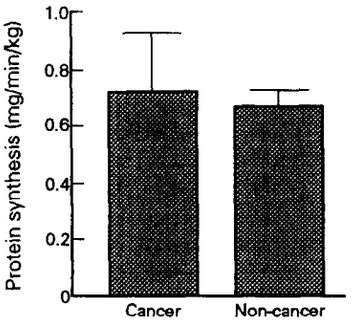

Fig. 3. Stimulated protein synthesis in cancer and non-cancer patients when rates of whole-body protein synthesis in fed state (200%) minus rate in fasted state are compared.

in both cancer and control patients (Table 2). RQ did not change in the cancer group on the low rate of TPN (120%) but was significantly increased by the high rate (200%). In the control group both rates of TPN increased RQ significantly. PREE overestimated resting expenditure in the control group, but it was close to expenditures during TPN infusions.

Tyrosine flux, oxidation and estimates of protein synthesis

Cancer patients as a group had increased whole-body tyrosine flux in the fasted state compared with non-cancer patients (Fig. 2). Whole-body tyrosine flux was not affected by the low TPN rate (120%) in any of the groups but increased significantly in all groups on the high TPN rate (Table 3). Tyrosine oxidation increased significantly in cancer patients both on the low and high TPN rate, while it only increased on the high TPN rate in the control group. Protein synthesis was not affected by the low TPN rate in any group, but increased significantly in both cancer and control patients on the high TPN rate. The degree of stimulation was similar in cancer and non-cancer patients (Fig. 3).

Arterial concentrations and leg exchange of aminoacids and substrates

Arterial concentrations of tyrosine were similar in all groups. The arterial concentration of tyrosine was not affected by any of the TPN rates, but the arterial concentration of the sum of all aminoacids was significantly increased by both the low and high TPN rate in all groups. This was also true for phenylalanine (results not shown). Although negative, the leg exchange of tyrosine in the fasted state showed high variability in all patient groups. The balance of tyrosine across the leg was significantly improved only in the group of cancer patients receiving 200%. The leg balance of total aminoacids did not improve significantly in any of the groups during TPN infusions (Table 4), but the branched-chain aminoacids were taken up in all the groups during TPN (cancer—120%, 334 (55); 200%, 440 (32); controls—120%, 337 (74); 200%, 457 (80) nmol/min per 100 g leg tissue; $P < 0.05$ compared with zero balance level).

Arterial concentrations of glucose, lactate, glycerol and FFA were not significantly different between the groups in the fasted state (Table 5). Arterial concentrations of glucose were significantly increased in all groups by the two TPN rates, while the lactate concentration was increased only by the high TPN rate in cancer and non-cancer patients. Glycerol concentrations were significantly increased by the high TPN rate only in the control group. The arterial concentrations of FFA were significantly reduced in all groups during TPN infusion.

Blood flow was not affected by TPN infusion, while plasma insulin concentration was increased significantly in all groups by TPN. Leg balances of glucose, lactate, glycerol and FFA in either the fasted or fed state did not differ between the four

Table 4. Arterial concentrations and leg exchange of tyrosine and total aminoacids in fasted and fed state

	Cancer		Control	
	120%	200%	120%	200%
Arterial concentration or tyrosine (μmol/l)				
Fasted	43 (4)	54 (6)	46 (5)	43 (7)
TPN	49 (9)	53 (9)	52 (4)	46 (5)
Balance of tyrosine (nmol/100 g/min)				
Fasted	−17 (33)	−68 (23)	−28 (17)	−32 (13)
TPN	6 (22)	−37 (28)*	−22 (34)	−28 (14)
Arterial concentration of sum of all aminoacids (μmol/l)				
Fasted	1760 (213)	1667 (122)	1884 (117)	1806 (143)
TPN	2675 (196)*	2370 (222)*	2576 (129)*	2878 (267)*
Balance of all aminoacids (nmol/100 g/min)				
Fasted	−536 (485)	−1268 (427)†	−535 (534)	−726 (204)†
TPN	98 (230)	−870 (560)	−103 (649)	−186 (512)

*$P < 0.05$, fasting vs. TPN.
†Significantly different from zero balance.

Table 5. Arterial concentrations in fasted and fed state

	Cancer		Control	
	120%	200%	120%	200%
Glucose (mmol/l)				
Fasted	4.6 (0.3)	4.6 (0.2)	5.0 (0.1)	4.7 (0.2)
TPN	6.7 (0.4)*	7.9 (0.5)*	7.4 (0.5)*	7.7 (0.7)*
Lactate (mmol/l)				
Fasted	0.66 (0.07)	1.1 (0.33)	0.56 (0.05)	0.57 (0.04)
TPN	0.90 (0.19)	1.24 (0.23)*	0.60 (0.05)	0.82 (0.08)*
Glycerol (μmol/l)				
Fasted	138 (7)	159 (28)	122 (8)	125 (22)
TPN	166 (17)	165 (18)	124 (16)	166 (23)*
FFA (mmol/l)				
Fasted	0.67 (0.07)	0.69 (0.14)	0.58 (0.05)	0.52 (0.05)
TPN	0.38 (0.05)*	0.29 (0.07)*	0.38 (0.06)*	0.30 (0.04)*

*$P < 0.05$, fasting vs. TPN.

Table 6. Blood flow and leg exchange in fasted and fed state

	Cancer		Control	
	120%	200%	120%	200%
Blood flow (ml/100 g/min)				
Fasted	4.2 (0.4)	4.4 (1.1)	3.0 (0.8)	3.2 (0.4)
TPN	4.1 (0.5)	4.8 (0.6)	3.0 (0.5)	4.1 (0.6)
Glucose balance (nmol/100 g/min)				
Fasted	−560 (407)	−89 (348)	−98 (104)	210 (164)
TPN	347 (908)	2869 (531)*	−160 (509)	1690 (531)*
Lactate balance (nmol/100 g/min)				
Fasted	−655 (158)	−1197 (363)	−549 (204)	−607 (86)
TPN	−391 (167)	−1495 (979)	−319 (65)	−608 (84)
Glycerol balance (nmol/100 g/min)				
Fasted	−343 (129)	−539 (262)	−140 (43)	−246 (71)
TPN	−290 (106)	−137 (50)	−102 (30)	−80 (106)
FFA balance (nmol/100 g/min)				
Fasted	−1105 (438)	−1664 (607)	−268 (410)	−835 (249)
TPN	−505 (346)	11 (85)	74 (346)	−224 (189)
Insulin arterial concentration (μU/ml)				
Fasted	4.9 (1.0)	3.4 (0.3)	4.2 (0.6)	5.5 (0.7)
TPN	16.2 (3.5)*	23.0 (5.0)*	18.6 (5.5)*	42.4 (10.2)*

*$P < 0.05$, fasting vs. TPN.

groups. Glucose balance was significantly increased by the high TPN rate in both cancer and control patients (Table 6). The lactate, glycerol and FFA balance did not change significantly in any of the patient groups by TPN although some alterations occurred, particularly depression of FFA release.

DISCUSSION

Due to the limited number of patients in this kind of laborious investigation, it was not possible to achieve absolute stratification of patients according to all variables that were regarded as potentially important. TSF was the only variable that was significantly different among the groups. No difference, however, was assumed to influence negatively our conclusions. On the contrary, we believe that the possibility that our cancer patients in general may have been more depleted than the control patients should reduce the risk for overinterpretation in regard to protein synthesis stimulation. The results showed that the cancer patients as a group had increased REE and elevated whole-body flux of tyrosine in the fasted state compared with the non-cancer patients. These results confirm our previous investigations [21, 22] and demonstrate that the present group of cancer patients was similar to those used in our previous studies in nutritional state and tumour–host metabolism.

We used the primed constant infusion of [^{14}C]tyrosine to measure feeding-induced stimulation of protein synthesis. Although tyrosine is a non-essential aminoacid it may be advantageous in this kind of dynamic experiment in man. The distribution volume of tyrosine is small, which leads to rapid equilibration with reasonable plateau levels of specific radioactivity within 2–2.5 h in both the plasma pool and expired carbon dioxide [12]. Tyrosine is not metabolised in the large skeletal muscle pool and is one of those aminoacids that are generally not switched into a balanced uptake across the periphery in the way that some aminoacids, especially those with branched chains, are [13, 14], which we confirmed in the present study. In addition, the enzymatic method that we are using for isolation and determination of the specific radioactivity of tyrosine in plasma allows a 5–6 fold higher amount of radioactivity in tyrosine to be isolated and counted compared with background levels when a dose as small (11.1 kBq) is infused.

We demonstrated that a standard TPN regimen does not stimulate protein synthesis in either malnourished cancer or non-cancer patients. Considerably higher TPN rates were necessary to achieve activation of overall whole-body protein synthesis but protein balance, especially in leg tissues, may still have been negative despite the high infusion rate. In this respect it appeared that cancer patients responded similarly to non-cancer patients. Our previous observations of insufficient nutritional effects to protect lean body mass in chemotherapy-treated cancer patients are, thus, also valid for cancer patients without previous drug treatment. It is therefore conceivable that a major defect can be ascribed to the nutrition regimen itself. If so, it is not surprising that previous investigations of standard nutrition in cancer patients have shown little, if any, impact on functional outcome.

Severe malnutrition results in lowered protein synthesis [23], although its relation to various degree of undernutrition is less established in man. Cortisol and catecholamines are also associated with impaired protein balance in peripheral tissues [24, 25] and probably with increased synthesis of some proteins in visceral tissues. We have reported that cachectic cancer patients have significantly increased glucocorticoid and catecholamine secretion compared with malnourished non-cancer patients [26]. In addition, adrenaline infusions revealed a significantly increased reactivity to adrenaline in cancer patients [27]. Although the relevance of such observations to the present findings is unclear, they do not seem to invalidate our conclusion since both cancer and non-cancer patients showed qualitatively the same negative whole-body response to standard nutrition and the same negative leg response to high nutrition rates. This study also confirms our findings [1] that the thermic effect of nutrition was not higher in cancer patients (about 9%) compared with non-cancer patients (about 17%), which has also been reported by others [28]. Our results thus imply that neither malnourished cancer nor non-cancer patients can ever restitute normal body composition when nourished with moderate TPN rates. Therefore, they should be more vigorously treated if already degraded proteins are to be resynthesised.

Even the high infusion rate of TPN (200%) did not support an overall tyrosine uptake across the leg while the balance of the branched-chain aminoacids was positive. The suggestion that even this high rate of TPN had low effectiveness in supporting anabolism in some protein compartments such as skeletal muscle, was, however, not obvious when comparing the exchange of the sum of all aminoacids across the periphery in the fed vs. fasted state (Table 4). Therefore, further studies are required before we can decide which aminoacid(s) is the most suitable marker to reflect protein balance across the leg. Our investigations suggest that methionine, tyrosine and phenylalanine are

such potential markers (unpublished). Although insulin levels were moderately changed in response to the high TPN rate, the fall in arterial FFA levels support the suggestion that lipolysis was significantly inhibited in other compartments than the leg. Insulin levels between 23–42 μU/ml in combination with elevated arterial glucose concentrations were also enough to stimulate glucose uptake across the leg at the high TPN infusion rate, although insulin resistance occurs in cancer patients [29, 30]. This may explain why the moderate TPN rate was insufficient to support a clear uptake of glucose across the leg.

In conclusion, a standard intravenous nutrition regimen was insufficient to stimulate protein synthesis in both undernourished cancer and non-cancer patients. Much higher TPN rates are necessary to use to obtain whole-body protein synthesis, but the degree of stimulation may still be low in peripheral leg tissues. This lack of feeding response was dependent on the nutrition regimen itself, since none of our patients had received previous chemotherapy or radiation treatment.

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