RESEARCH LETTER

# Stratification of cardiovascular disease risk in adults receiving long-term home parenteral nutrition

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**Introduction** Many studies suggest that diet significantly influences the risk of cardiovascular disease (CVD) and has a fundamental role in its prevention.[1,2] Nutrition affects CVD risk directly through physiological, molecular, and biological changes, which may trigger inflammation and oxidative stress.[3]

The aim of parenteral nutrition (PN) is to provide, through intravenous administration, adequate amounts of amino acids, glucose, lipids, electrolytes, vitamins, trace elements, and water to prevent malnutrition. The amount of individual components in the PN admixtures is strictly controlled for each patient. For this reason, patients requiring long-term PN are a unique population with a controlled micro- and macronutrient provision.[4]

There are several methods to assess CVD risk, and some of them were adapted for selected groups of patients.[5] There are no recommendations for CVD risk assessment in individuals receiving long-term PN. Risk stratification results based on the commonly used tools can be affected by clinical and biochemical changes associated with long-term PN.

The aim of the study was to assess the differences in CVD risk in patients receiving long-term home PN (HPN), estimated using the following methods: (i) C-reactive protein (CRP) serum level; (ii) the 2018 Pooled Cohort Equation (PCE) ASCVD 10-year Risk Calculator, and (iii) the Systematic Coronary Risk Evaluation (SCORE).

**Patients and methods** Patients receiving PN (study group) and healthy volunteers (control group) were recruited over a period of 7 months. The inclusion criteria for the study group were as follows: (1) HPN for at least 6 months, (2) age, 50–79 years, (3) a diagnosis of short bowel syndrome, and (4) no less than 3 days of PN per week. The exclusion criteria comprised (1) a history of CVD, (2) age over 79 years, (3) terminal illness, or (4) refusal or inability to give informed consent.

Information about lifestyle behaviors, diabetes status, and a history of hypertension was obtained via a questionnaire.

Physical measurements of height, weight, and blood pressure were taken. Serum levels of CRP, total and high-density lipoprotein (HDL) cholesterol, and triglycerides were tested. Repeated measurements of CRP and total cholesterol serum levels were performed in the study group. The follow-up examinations were part of standard care in that group of patients. Data from the period between April 2015 and April 2021 were analyzed. The cutoff point for CRP as a marker of CVD was established at 3 mg/l (low / moderate risk, <3 mg/l; elevated risk, ≥3 mg/l).[6]

The online PCE CV Risk Calculator was used to estimate the 10-year risk for atherosclerotic CVD (ASCVD) (https://framinghamheartstudy.org/fhs-risk-functions/cardiovascular-disease-10-year-risk/). For each participant, information on age, sex, systolic blood pressure (SBP), antihypertensive treatment, history of diabetes, treatment with statins, smoking status, aspirin therapy, as well as total and HDL cholesterol serum levels was entered into the calculator. The summation of points assigned to each of these variables resulted in a continuous score estimating the risk for developing ASCVD in the next 10 years. The equation for non-Hispanic white race was used. Low risk was defined as a 10-year ASCVD risk of less than 5%; borderline / intermediate risk, as 5% to 19.9%; and high risk, as 20% or greater.[7]

The SCORE system was used to estimate the 10-year risk of a fatal atherosclerotic event. The SCORE chart assessment is based on the following risk factors: age, sex, SBP, total cholesterol level, and smoking status.[8] A version of the risk chart for the high-risk population was used.[9] Low risk was defined as <1%; moderate, as ≥1% and <5%; high, as ≥5% and <10%, and very high, as ≥10%.

**Statistical analysis** Mean values with SD and medians with interquartile ranges (IQRs) were computed for continuous variables. Comparisons between the 2 groups were performed using the *t* test for independent variables, the $\chi^2$ test for smoking status and diabetes history, the Kolmogorov–Smirnov test for the SCORE values, and the Mann–Whitney test for the PCE results and triglycerides / CRP levels (nonnormal distribution). PAWS Statistic 18 (SPSS Inc, Chicago, Illinois, United States) was used to perform statistical analyses. A *P* value of less than 0.05 was considered significant.

All study participants signed an informed consent form prior to enrolment in the study. The study was approved by the Bioethics Committee of the Center of Postgraduate Medical Education (approval no. 46/PB/2017).

**Results** A total of 24 HPN patients (12 men and 12 women) from 270 individuals treated at the outpatient clinic of the Department of General Surgery and Clinical Nutrition met the inclusion criteria and entered the study. The control group included 24 healthy volunteers (11 men, 13 women). The study results are summarized in **TABLE 1**. The study and control groups were matched for baseline characteristics of age, body mass index, as well as smoking and diabetes statuses.

The indications for PN were as follows: mesenteric vascular events (n = 10), complications of noninflammatory bowel disease or noncancer abdominal surgery (n = 5), inflammatory bowel disease (n = 3), and others (n = 5). A single patient had a history of cancer (a long-term survivor with 6390 days of PN).

All participants in the study group were put on individualized PN mixtures. Various formulations of lipid emulsions were used in the PN combinations: 13 patients were given an emulsion with soybean oil (Intralipid; Fresenius Kabi AB, Uppsala, Sweden); 7 patients, an emulsion with a combination of fish, soybean, olive, and coconut oils (SMOFLipid; Fresenius Kabi AB); and 4 patients, an emulsion based on olive and soybean oils (ClinOleic; Baxter Ltd, Warsaw, Poland). Oral feeding covered between 5% and 50% of the nutritional needs of HPN patients.

The repeated measurements of CRP and total cholesterol serum levels were performed within a mean (SD) of 1800.08 (450.85) days. Single-point CRP results classified 12 PN patients (50%) as low- or moderate-risk. Based on the median value of the repeated CRP measurements, 2 PN patients (8.3%) were classified as low- or moderate-risk. According to the PCE and SCORE results, among the HPN individuals there were 7 (29.2%) and 4 patients (16.7%) in the low-risk group, 15 (62.5%) and 14 patients (58.3%) in the borderline / intermediate / moderate-risk group, and 2 (8.3%) and 6 patients (25%) in the high-risk group, respectively. Repeated long-term measurments of total cholesterol levels did not affect risk stratification of HPN patients based on the SCORE results and changed the risk group qualification based on the PCE in a single patient from high to intermediate risk (20.2% vs 19.7%).

**Discussion** Patients receiving long-term PN have good control of lipid intake. The production of cholesterol is impaired in this population. In particular, the serum lathosterol-to-cholesterol ratio is significantly lowered, resulting in reduced cholesterol production.[10]

As in other chronic states, CVD risk in PN patients is related to a combination of traditional cardiovascular risk factors and disease-specific factors. The latter could increase or decrease the CVD risk. In our study, the relatively low serum level of total cholesterol in PN patients could result in their qualification to a group with lower CVD risk according to SCORE and PCE.

Currently, there is limited information about blood pressure changes in patients receiving long-term HPN. In the present study, we found that SBP was lower in HPN patients compared with healthy controls. The PN formula contains lipids, which could potentially explain the reduced blood pressure.[11,12] Furthermore, the reduced SBP in HPN patients could also affect the SCORE and PCE results.

We found no literature data regarding CVD risk assessment in long-term PN patients. Although PN is applied due to serious medical conditions, many patients on long-term PN live for over 10 years with an improved quality of life (with some receiving the therapy for up to 30 years).[13]

In the presented study group of 24 HPN patients, a single episode of CVD was noticed. It was an ischemic stroke in a 63-year-old woman (total duration of PN, 9384 days) with moderate risk based on the SCORE assessment, low risk according to the PCE, and elevated risk according to both single-point and repeated measurements of the CRP level.

The paucity of literature data on CVD risk in HPN patients is likely due to the fact that CVD events are uncommon in this population, and it is difficult to draw conclusions based on data from a single center. A growing population of long-term PN patients with a survival time of more than 10 years would benefit from proper CVD risk stratification. Therefore, taking PN-specific risk factors into consideration should allow more accurate CVD risk stratification, as is the case with other diseases.[14,15]

The main limitation of the present study is the relatively small size of the study group. There

**TABLE 1** Baseline characteristics of the study cohort and the main study findings

| Parameter | Study group (n = 24) | | | Control group (n = 24) | | | *P* value |
|---|---|---|---|---|---|---|---|
| | Mean (SD)/n[a] | Median (IQR) | Range | Mean (SD)/n[a] | Median (IQR) | Range | |
| Age, y | 62.25 (5.06) | 60.5 (58.75–65.5) | – | 61.83 (5.82) | 62.5 (57–66) | – | 0.79[b] |
| BMI, kg/m$^2$ | 22.77 (2.80) | 22.82 (20.73–24.14) | – | 24.01 (1.75) | 23.73 (22.53–25.38) | – | 0.07[b] |
| Cigarette smoking, yes/no, n | 13/11 | – | – | 11/13 | – | – | 0.56[c] |
| Diabetes, yes/no, n | 1/23 | – | – | 1/23 | – | – | 1[c] |
| PCE | 9.02 (7.81) | 6.65 (4.9–10.9) | 1.5–38.3 | 16.65 (13.37) | 14.2 (5.82–26.7) | 0.8–52 | 0.056[d] |
| SCORE | 3.79 (2.69) | 2.0 (2.0–5.25) | 1–9 | 5.04 (4.88) | 3.0 (1.75–8.25) | 1–21 | 0.03[e] |
| Total cholesterol, mg/dl | 136.04 (41.53) | 135.5 (104.0–165.75) | 76–209 | 221.38 (40.81) | 220.0 (208.5–239.25) | 124–297 | 0.0001[b] |
| HDL cholesterol, mg/dl | 44.87 (13.03) | 42.85 (39.32–48.4) | 28.6–93.2 | 77.04 (23.91) | 72.15 (64.47–88.95) | 41.5–129.7 | 0.0001[b] |
| Triglycerides, mg/dl | 130.79 (92.12) | 100.5(75.5–162.0) | 30–406 | 97.598(0.82) | 88.0 (59.5–117.5) | 31–329 | 0.23[d] |
| CRP, mg/l | 16.57 (46.03) | 3.26 (2.27–8.57) | 1.15–223.98 | 5.10 (3.66) | 4.22 (2.9–4.98) | 1.19–17.16 | 0.74[d] |
| SBP, mm Hg | 122.21 (20.6) | 126.0 (107.5–132.5) | 90–165 | 137 (20.82) | 133.5 (125.12–151.25) | 101–190 | 0.014[b] |
| DBP, mm Hg | 76.33 (9.96) | 75.0 (69.5–82.5) | 60–96 | 86.89 (12.69) | 88.0 (76.0–91.62) | 66–112 | 0.002[b] |
| Duration of PN, d | 3510 (2858.9) | 2522.5 (1306–4759) | 671–9384 | – | – | – | – |
| Age at PN initiation, y | 54.0 (10.2) | 55.5 (50–62) | 33–69 | – | – | – | – |
| Weekly lipid dosage, g | 151.5 (48.8) | 140 (140.0–157.5) | 60–280 | – | – | – | – |
| Weekly amino acids dosage, g | 324.79 (57.43) | 350 (350–350) | 150–350 | – | – | – | – |
| Repeated measurements of CRP, n | 31.62 (12.55) | – | 14–68 | – | – | – | – |
| Repeated measurements of total cholesterol, n | 22.87 (5.31) | – | 12–31 | – | – | – | – |

a Data are presented as mean (SD) unless otherwise indicated.

b Compared with the *t* test

c Compared with the $\chi^2$ test

d Compared with the Mann–Whitney test

e Compared with the Kolmogorov–Smirnov test

SI conversion factors: to convert cholesterol to mmol/l, multiply by 0.0259; triglycerides to mmol/l, by 0.0113.

Abbreviations: BMI, body mass index; CRP, C-reactive protein; DBP, diastolic blood pressure; HDL, high-density lipoprotein; IQR, interquartile range; PCE, Pooled Cohort Equations Cardiovascular Risk Calculator; PN, parenteral nutrition; SBP, systolic blood pressure; SCORE, Systematic COronary Risk Evaluation

was only a limited number of long-term HPN patients in a single center. This is widely reflected in many publications on this topic. Differences in the etiology of short bowel syndrome in the HPN patients is another study limitation. In some patients, the etiology could impact the CVD risk. The relatively small number of long-term HPN patients makes it difficult to find homogeneity in the etiology of short bowel syndrome and, consequently, an appropriately sized group.

To conclude, 92% of adult patients on long-term PN were categorized into the low or intermediate CVD risk group according to the PCE results, 75% according to the SCORE assessment, 50% according to the single-point CRP measurements, and only 8% according to repeated CRP measurements. Repeated long-term measurments of total cholesterol levels did not change the SCORE risk group qualification of the HPN patients and changed the PCE risk group qualification in a single patient from high to intermediate risk.

## ARTICLE INFORMATION

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## REFERENCES

1 Anand SS, Hawkes C, de Souza RJ, et al. Food consumption and its impact on cardiovascular disease: importance of solutions focused on the globalized food system: a report from the workshop convened by the World Heart Federation. J Am Coll Cardiol. 2015; 66: 1590-1614.

2 Guligowska AR, Pigłowska M, Śmigielski J, Kostka T. Inappropriate pattern of nutrient consumption and coexistent cardiometabolic disorders in elderly people from Poland. Pol Arch Med Wewn. 2015; 125: 521-531.

3 Rychter AM, Ratajczak AE, Zawada A, et al. Non-systematic review of diet and nutritional risk factors of cardiovascular disease in obesity. Nutrients. 2020; 12: 814.

4 Pironi L, Boeykens K, Bozzetti F, et al. ESPEN guideline on home parenteral nutrition. Clin Nutr. 2020; 39: 1645-1666.

5 van der Leeuw J, van Dieren S, Beulens JW, et al. The validation of cardiovascular risk scores for patients with type 2 diabetes mellitus. Heart. 2015; 101: 222-229.

6 Parrinello CM, Lutsey PL, Ballantyne CM, et al. Six-year change in high-sensitivity C-reactive protein and risk of diabetes, cardiovascular disease, and mortality. Am Heart J. 2015; 170: 380-389.

7 Goff DC Jr, Lloyd-Jones DM, Bennett G, et al. 2013 ACC/AHA guideline on the assessment of cardiovascular risk: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. Circulation. 2014; 129: S49-S73.

8 Conroy RM, Pyörälä K, Fitzgerald AP, et al. Estimation of ten-year risk of fatal cardiovascular disease in Europe: the SCORE project. Eur Heart J. 2003; 24: 987-1003.

9 Piepoli MF, Hoes AW, Agewall S, et al. 2016 European Guidelines on cardiovascular disease prevention in clinical practice: the Sixth Joint Task Force of the European Society of Cardiology and Other Societies on Cardiovascular Disease Prevention in Clinical Practice (constituted by representatives of 10 societies and by invited experts) Developed with the special contribution of the European Association for Cardiovascular Prevention & Rehabilitation (EACPR). Eur Heart J. 2016; 37: 2315-2381.

10 Carulli L, Del Puppo M, Anzivino C, et al. In vivo degradation of cholesterol to bile acids is reduced in patients receiving parenteral nutrition. JPEN J Parenter Enteral Nutr. 2014; 38: 220-226.

11 Santarpia L, Esposito R, Vaccaro A, et al. Cardiac changes in patients on long-term parenteral nutrition. Nutrients. 2019; 11: 1587.

12 DiNicolantonio JJ, OKeefe J. Dietary fats, blood pressure and artery health. Open Heart. 2019; 6: e001035.

13 Tsang PY, Carey S. Impact of home parenteral nutrition on daily life: a qualitative study of eight patients. Nutr Diet. 2015; 72: 16-21.

14 Dibb M, Soop M, Teubner A, et al. Survival and nutritional dependence on home parenteral nutrition: three decades of experience from a single referral centre. Clin Nutr. 2017; 36: 570-576.

15 Calcaterra I, Tufano A, Lupoli R, et al. Cardiovascular disease and antiphospholipid syndrome: how to predict and how to treat? Pol Arch Intern Med. 2021; 131: 161-170.