Determinants of the hyperdynamic circulation and central hypovolaemia in cirrhosis

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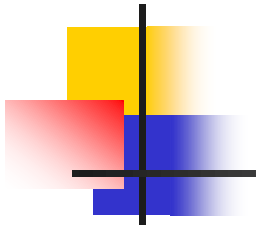
Objective On the basis of a large population of patients with cirrhosis to identify splanchnic and clinical characteristics associated with the development of the hyperdynamic circulation and survival.



Methods We included 410 patients with cirrhosis. In all patients, a full haemodynamic investigation was performed. The data were analysed using regression analyses, principal components analyses, and Cox proportional hazards analyses.

Patients

- 410 patients with cirrhosis
- 372 alcoholic, 38 post.hep., 10 cryp. or mixed
- 290 males, 120 females
- Child-Turc. A 108, B 186, C 116
- Ascites in 233

Variables studied (1)

Patient characteristics

- Gender (M/F)
- Age (years)
- Body height (cm)
- Body mass index (kg/m^2)
- Ideal body weight (kg)
- Body surface area (m^2)
- Lean body mass (kg)
- Fat body mass (kg)
- Bone mineral content (kg)
- Ascites (+/−)
- Presence of oesophageal varices
- Child class (A/B/C)
- Child score

Biochemistry

- B-haemoglobin (mmol/l; 8.1—10.3)
- P-coagulation factors 2, 7 and 10 (units; 0.70—1.30)
- S-alanine aminotransferases (U/l; 10—40)
- S-alkaline phosphatases (U/l; 50—275)
- S-albumin (μmol/l; 540—800)
- S-bilirubin (μmol/l; 2—17)
- S-sodium (mmol/l; 136—146)
- S-creatinine (μmol/l: <120)
- Arterial oxygen tension (kPa)
- Arterial oxygen saturation (%)
- Alveolar—arterial oxygen gradient (mm Hg)

Variables studied (2)

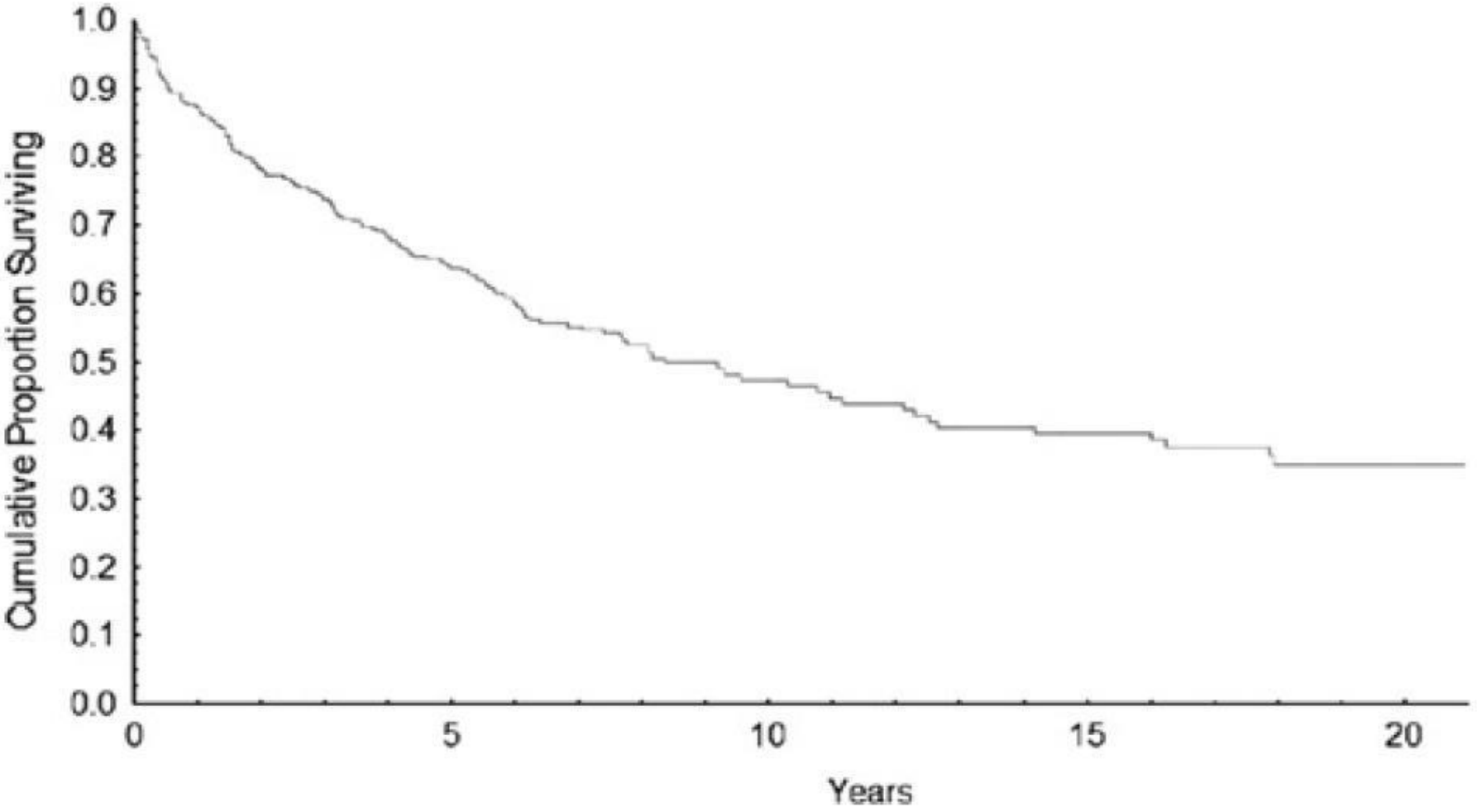
Systemic haemodynamics

- Systemic vascular resistance ($dyn \cdot s \cdot cm^{-5}$; 1600—2300)
- Arterial compliance (mm Hg/ml)
- Right atrial pressure (mm Hg; <5)
- Heart rate (/min)
- Cardiac output (l/min)
- Stroke volume (ml)
- Pulse pressure (mm Hg)
- Arterial compliance (mm Hg/ml)
- Central circulation time (s, 14—28)
- Central blood volume (ml/kg)
- Plasma volume (ml/kg)
- Blood volume (l)
- Non-central blood volume (l)

Splanchnic haemodynamics

- Wedged hepatic venous pressure; (mm Hg<15)
- Free hepatic venous pressure (mm Hg; <7)
- Hepatic venous pressure gradient (mm Hg: <5)
- Hepatic blood flow (l/min, 0.5—2.3)
- Post-sinusoidal resistance ($dyn \cdot s \cdot cm^{-5}$; <370)
- ICG clearance (ml/min; 300—700)
- Galactose elimination capacity (mmol/min; F>1.4; M>1.7)
- Systolic blood pressure (mm Hg)
- Diastolic blood pressure (mm Hg)
- Mean arterial blood pressure (mm Hg)

Survival


Cumulative Proportion Surviving
1.0
0.9
0.8
0.7
0.6
0.5
0.4
0.3
0.2
0.1
0.0
0
5
10
15
20
Years

Principal Components Analysis (factor analysis)

- This method analyses the correlation pattern between the variables
- ***It combines groups of highly correlated variables***
- This results in a smaller number of independent (uncorrelated) new variables (components or factors) explaining a large part of the variation.
- The purpose is ***to clarify the structure*** in the data

Principal components (factors)

- We obtained 9 principal components accounting for 75.3 % of the variance in the data.

Factor 1	Body dimensions
Factor 2	Liver dysfunction
Factor 3	Systemic haemodynamics
Factor 4	Body volume
Factor 5	Central haemodynamics
Factor 6	Arterial oxygenation
Factor 7	Right cardiac preload
Factor 8	Central hypovolaemia
Factor 9	Splanchnic haemodynamics

Factor	1. Body dimensions
Variable	
Body height	**0.90**
IBV (Ideal Body Weight)	**0.90**
BSA (Body Surface Area)	**0.79**
Male gender	**0.75**
LBM (Lean Body Mass)	**0.69**
BMC (Bone Mineral content)	**0.59**

Variance explained (%) 21.36

Factor	2. Liver dysfunction
Variable	
Child score	**0.87**
S-albumin	**-0.74**
S-bilirubin	**0.71**
CF 2.7.10	**-0.69**
Ascites	**0.64**
HVPG	**0.61**
WHVP	**0.60**
ICG clear.	**-0.55**

Variance explained (%) 13.83

Factor	3. Changes In systemic circulation
Variable	
Systolic BP	**0.97**
Mean Arterial P	**0.87**
Pulse pressure	**0.83**
Diastolic BP	**0.68**

Variance explained (%) 8.66

Factor	4. Body volume
Variable	
BMI (body mass index)	**0.85**
FBM (total fat mass)	**0.72**
PV (plasma volume)	**-0.60**

Variance explained (%) 7.35

Factor	5. Central haemodynamics
Variable	
CI (cardiac index)	**0.90**
CO (cardiac output)	**0.89**
SV (stroke volume)	**0.79**
SVR (systemic vasc. res.)	**-0.78**
AC (arterial compliance)	**0.63**
BV (blood volume)	**0.59**
non-Central Blood Vol.	**0.58**

Variance explained (%) 6.67

Factor	6. Arterial oxygenation
Variable	
PaO2	**-0.95**
AaPO2 (alv.-art. O-grad)	**0.91**
O2 SAT	**-0.86**

Variance explained (%) 5.65

Factor	7. Right heart preload
Variable	
Free Hep. Ven. Pressure	**0.85**
Right Atrial Pressure	**0.81**

Variance explained (%) 4.47

Factor	8. Central
	hypovolemia
Variable	
Central Blood Volume	**0.83**
Central Circulation Time	**0.56**

Variance explained (%) 4.02

Factor	9. Splancnic haemo-dynamics
Variable	
Post-Sinusoidal Resist.	**-0.88**
Hepatic Blood Flow	**0.76**

Variance explained (%) 3.28

Table 6 Regression coefficients, standard errors (SE) and p-values of the proportional hazard Cox regression analyses for factor scores for each principal component

Variable	Description of factor	Reg. coeff.	SE	p Value
Factor 1	Body dimensions	−0.015	0.080	0.8
Factor 2	Liver dysfunction	0.290	0.073	0.00007
Factor 3	Systemic haemodynamics	0.038	0.083	0.6
Factor 4	Body volume	−0.031	0.077	0.6
Factor 5	Central haemodynamics	0.044	0.076	0.5
Factor 6	Arterial oxygenation	0.042	0.078	0.5
Factor 7	Right cardiac preload	−0.224	0.081	0.005
Factor 8	Central hypovolaemia	0.118	0.075	0.1
Factor 9	Splanchnic haemodynamics	−0.020	0.076	0.7

Conclusions

- Principal components can clarify the structure of complex data
- A reduced number of independent factors can be identified
- The marked prognostic influence of hepatic dysfunction was confined to one factor
- The independent factor of reduced cardiac preload had additional prognostic influence