DNA immediately after exhaustive exercise and its disappearance within 2 h after the race suggests that cell-free plasma DNA could possibly be an important tool for monitoring and quantification of cellular damage. Experiments are ongoing in our laboratories to determine whether apoptotic or necrotic events are responsible for the observed phenomenon. Although it seems likely that the source of cell-free plasma DNA is the skeletal muscle cell, further investigations are needed to determine whether other cell types are involved as well.

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References


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indicator of ventricular recovery during mechanical support. Milting et al. (8) studied both A-type natriuretic peptide (ANP) and BNP in 24 patients with end-stage heart failure supported by four different types of LVADs. They concluded that the decreases in ANP and BNP with time after implantation was dependent on LVAD type, which should be taken into consideration when selecting patients that could be weaned from the LVAD without heart transplantation.

To our knowledge the current study is the first in which both BNP and NT-proBNP were monitored in patients after unloading of the left ventricle by use of a LVAD. We examined plasma samples of 15 patients (13 males and 2 females; mean age; 44 years; age range, 16–63 years) with end-stage heart failure at the time of LVAD implantation. Cardiomyopathy was the underlying cause in nine patients and ischemic heart disease in six patients. To avoid variation in results attributable to the use of different device types (8), only patients supported by a Heartmate (Thoratec) were included in the study. None of the patients could be weaned from the LVAD, and all patients were transplanted. The mean time to transplantation was 284 days (range, 124–557 days). Blood samples were taken just before implantation and 1 week, 1 month, and 3 months after implantation. Indication for implantation of a LVAD was cardiogenic shock refractory to drug treatment. After implantation there is a rapid normalization of hemodynamics and improvement of end-organ dysfunction and exercise tolerance (9). Most patients are allowed to go home and have a reasonable quality of life with a low incidence of major adverse events.

Although BNP and NT-proBNP are synthesized in a 1:1 ratio, their plasma concentrations are different because of their different half-lives in vivo. BNP is cleared mainly from the circulation by the natriuretic peptide C receptor and degraded by neutral endopeptidase, whereas NT-proBNP is cleared by the kidneys (4). Therefore, NT-proBNP concentrations inversely correlate with the glomerular filtration rate and increase with age. The half-life of BNP is only 22 min, whereas the half-life of NT-proBNP is much longer, ~120 min with a normal glomerular filtration rate. In vitro, BNP is less stable than NT-proBNP if blood is not collected in plastic tubes containing EDTA as an anticoagulant (10, 11).

In this study BNP was analyzed on an ADVIA Centaur immunochemistry system (Bayer Diagnostics) and NT-proBNP on an Elecsys immunochemistry system (Roche Diagnostics). All blood samples were collected by venipuncture in plastic EDTA tubes and centrifuged within 30
min, and plasma was stored in plastic tubes at −20 °C until analysis.

Overall there was good correlation between BNP and NT-proBNP in this specific group of heart failure patients both before and after implantation of a LVAD \((y = 2.45x^{1.09}, R^2 = 0.89; \text{Fig. 1A})\). Panels B and C in Fig. 1 show BNP and NT-proBNP values over time for individual patients. All 15 patients had increased BNP \([\text{mean (SD)} = 1979 (1052) \text{ng/L} \text{and NT-proBNP} [21 485 (11 633) \text{ng/L} \text{concentrations before implantation. One week after implantation of the LVAD, both BNP and NT-proBNP had decreased dramatically \([283 (131) \text{ng/L and 3095 (2111)} \text{ng/L, respectively}\]. In contrast to the results reported by Sodian et al. \((7)\), the early decreases in BNP and NT-proBNP correlated with the unloading of the left ventricle but were not indicative of ventricular recovery. Between 1 week and 1 month after implantation, both BNP and NT-proBNP seemed to stabilize \([321 (307) \text{ng/L and 4171 (8182)} \text{ng/L, respectively}\], followed by a further decrease between 1 month and 3 months after implantation \([\text{BNP}, 124 (90) \text{ng/L;} \text{NT-proBNP, 984 (789)} \text{ng/L} \text{. This is different from an earlier report \((8)\) in which not all patients supported by a Heartmate reached BNP concentrations within the reference interval. However, one patient showed, after an initial decrease, a marked increase in both BNP and NT-proBNP between 1 week and 1 month after implantation, followed by normalization at 3 months after implantation \((\text{Fig. 1, B and C})\). The increased BNP and NT-proBNP concentrations 1 month after implantation could be the result of repetitive ventricular tachycardia in this patient at that time. As mentioned, implantation of a LVAD leads to normalization of hemodynamics and an improvement in end-organ dysfunction. All patients except this one showed a distinct improvement in renal function leading to normalization of the estimated glomerular filtration rate \((\text{eGFR})\), according to Cockcroft and Gault \((12)\), within 1 week after implantation \((\text{data not shown})\).

The preimplantation BNP concentrations were approximately twice as high as reported BNP concentrations of NYHA class IV patients, whereas the NT-proBNP concentrations were 10 times higher than the reported concentrations in NYHA class IV patients \((2, 4)\). In addition to the fact that our patients are the sickest among NYHA class IV patients, the most likely explanation for this discrepancy is that most of them had preimplantation renal dysfunction \((\text{mean eGFR, 60 mL/min; range, 30–133 mL/min})\), which in turn led to reduced renal clearance of NT-proBNP compared with “normal” NYHA class IV patients. BNP, which is cleared mainly by a specific receptor, is therefore less influenced by renal function. Indeed, by plotting the NT-proBNP/BNP ratio against the eGFR, we could show that the NT-proBNP/BNP ratio increased when the eGFR decreased to <80 mL/min \((\text{Fig. 1D})\). These observations are in line with the results reported by McCullough et al. \((13)\) showing that in patients with congestive heart failure with BNP concentrations >500 ng/L, BNP is not increased as a result of a decreased glomerular filtration rate. In contrast, NT-proBNP concentrations correlate with the glomerular filtration rate independently of overload of the left ventricle \((4)\).

In conclusion, both plasma BNP and NT-proBNP concentrations correlate well with the unloading of the left ventricle and the clinical improvement over time of patients with end-stage heart failure who received a LVAD to bridge the time to transplantation. On the basis of our results, overestimation of NT-proBNP must be considered in patients with severe renal dysfunction.

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**References**


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