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D. Jain, M. Grimm, C. Bartels1, M. Bechtel1, R. Tölg, F. Hartmann, H. A. Katus, H. H. Sievers1, G. Richardt

Results of endoaneurysmorrhaphy (EAR) have been followed haemodynamically and functionally. Since heart failure and myocardial infarctions with left ventricular (LV) dysfunction are associated with prognostically significant neurohumoral activation, we sought to study patients undergoing EAR haemodynamically and neurohumorally in the early post-operative period. Arterial plasma levels of N-terminal pro-atrial natriuretic peptide (Nt-proANP), N-terminal pro-brain natriuretic peptide, arginine vasopressin (AVP), endothelin, norepinephrine and epinephrine were measured before and early postoperatively (day 6–21; median 8.5) in 11 patients undergoing EAR. Pre- and postoperative haemodynamic and angiographic examination was carried out in all patients. Ejection fraction improved from 31.7 ± 4.3 to 48.2 ± 4.4 % (p < 0.005) after surgery. Left ventricular end-diastolic pressure (LVEDP) increased significantly from 11.3 ± 2.4 to 19.1 ± 3.5 mmHg (p < 0.05). The Nt-proANP levels also increased significantly from 1121 ± 219 to 1921 ± 190 fmol/ml (p < 0.005). Postoperatively, LVEDP showed a positive correlation with plasma Nt-proANP (r = 0.73, p = 0.01). There appears to be a discordance in LV pump functions early postoperatively. An improvement in systolic performance is accompanied by a worsening of diastolic function. This is further substantiated by an increase in Nt-proANP, a bad prognostic marker. The results are, however, preliminary.

Keywords: aneurysm, revascularisation, myocardial infarction, haemodynamics, hormones

Formation of left ventricular aneurysms is not uncommon after myocardial infarction [1]. Surgical excision is carried out to improve the clinical manifestations, most often heart failure, but sometimes angina, embolization, and life-threatening tachyarrhythmias [2, 3]. The operation has evolved from conventional aneurysmectomy, ie repair with linear plication of the aneurysm sac to the present day techniques of aneurysmorrhaphy, which emphasize the restoration of normal left ventricular geometry [1, 4]. It has been customary to follow-up these cases haemodynamically and functionally. Thus literature is replete with reports of improvement in left ventricular ejection fraction and New York Heart Association (NYHA) class. Since heart failure and large myocardial infarctions are associated with significant neurohumoral activation [5, 6], it would be of interest to have a neurohumoral follow-up of these patients. If the surgery improves left ventricular functions, it must have an effect on the neurohumoral profile. We sought to have a short term haemodynamic, angiographic and neurohumoral follow-up of patients undergoing endoaneurysmorrhaphy, and in doing so attempted to find out changes which could have a bearing on the ultimate outcome of the operation.

Methods

Eleven patients were studied early postoperatively (day 6–21; median 8.5). All had congestive heart failure and anterior left ventricular aneurysm. In every case the aneurysm resulted from myocardial infarction. Indications for operation were congestive heart failure and/or angina pectoris. Co-morbid risk factors like hypertension, diabetes mellitus, atrial fibrillation, mitral regurgitation, ventricular arrhythmias were present in some patients. All patients were receiving decongestive treatment in the form of diuretics, angiotensin-converting enzyme inhibitors, angiotensin receptor antagonists, low dose beta-blockers, etc. and all gave written informed consent. Cooley’s surgical technique was followed, the details of which have been cited in [7]. Intracardiac pressures were obtained during cardiac catheterisation and quantitative left ventriculography (QLVACMS, Medis Medical Imaging Systems, Leiden, Holland) was employed to derive the angiographic data. Global left ventricular ejection fraction was calculated by the area-length method. Arterial blood was collected after coronary angiography. It was centrifuged within 20 minutes and the separated plasma was stored at –80 degree centigrade until assayed. A competitive enzyme immuno assay (EIA, Bio- medica GmbH, Vienna, Austria) was used to measure the immunoactive N-terminal proatrial natriuretic peptide (Nt-proANP) (1–30) and N-terminal pro-brain natriuretic peptide (Nt-proBNP) (8–29). Norepinephrine and epinephrine were quantified by high-pressure liquid chromatography (HPLC) and electrochemical detection. Commercially available enzyme linked immunosorbsent assay (ELISA, Biomedica GmbH Vienna, Austria) was used to measure endothelin. Quantitative determination of arginine vasopressin was done by using a competitive enzyme immunoassay (Assay Designs, Inc., Ann Arbor, U.S.A.). Data are presented as mean ± S.E.M. Paired t-test was used for comparisons between pre- and postoperative parameters in patients. Bivariate Pearson analysis for correlations was done by SPSS software from SPSS Inc. A p-value of < 0.05 was used to indicate statistical significance.

Results

The results are summarized in Tables 1 and 2. Stroke volume showed an insignificant rise, though on subgroup analysis a differential pattern emerged, with a significant rise from 37 ± 8 to 61 ± 9 ml (n = 6, p = 0.02) in patients having low preoperative stroke volumes ≤ 70 ml, and a rather insignificant fall (33 ± 12 vs. 67 ± 8, n = 5; ns) in patients having higher (> 70 ml) preoperative stroke volumes. In the latter group, the postoperative rise of the ejection fraction may have resulted from myocardial infarction [1]. Surgical excision is carried out to improve the clinical manifestations, most often heart failure, but sometimes also angina, embolization, and life-threatening tachyarrhythmias [2, 3]. The operation has evolved from conventional aneurysmectomy, ie repair with linear plication of the aneurysm sac to the present day techniques of aneurysmorrhaphy, which emphasize the restoration of normal left ventricular geometry [1, 4]. It has been customary to follow-up these cases haemodynamically and functionally. Thus literature is replete with reports of improvement in left ventricular ejection fraction and New York Heart Association (NYHA) class. Since heart failure and large myocardial infarctions are associated with prognostically significant neurohumoral activation [5, 6], it would be of interest to have a neurohumoral follow-up of these patients. If the surgery improves left ventricular functions, it must have an effect on the neurohumoral profile. We sought to have a short term haemodynamic, angiographic and neurohumoral follow-up of patients undergoing endoaneurysmorrhaphy, and in doing so attempted to find out changes which could have a bearing on the ultimate outcome of the operation.

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context. This apparent dichotomy of improvement in ejec-
tion performance and worsening of diastolic function is the principal finding of our study.

The observation is further substantiated by a significant
rise in Nt-proANP post-operatively. A significant correlation
was found between LVEDP and Nt-proANP (figure 1),
much in conformity with Takeichi et al., who found a linear
relation between plasma ANP levels, and pulmonary cap-
illary wedge pressure and also between LVEDP and maximal
left atrial volume [12]. The Nt-proANP has been shown to
be an independent predictor of cardiovascular mortality and
the development of heart failure following myocardial infarc-
ction [6, 13]. In a multivariate analysis Nt-proANP in contrast
to ANP and other neurohormones was found to be a power-
ful and independent predictor when the model included age,
gender, prior myocardial infarction, hypertension, diabetes,
use of thrombolysis, Killip class, infarct location, and left ven-
tricular ejection fraction. For the combined end-point of car-
diovascular death or severe heart failure, Nt-proANP was the
best clinical or laboratory predictor, even superior to age, left
ventricular ejection fraction and prior myocardial infarction
[6]. As increasing filling pressures are a major stimulus for
centric ventricular hypertrophy [14] increased atrial pres-
sure suggested by elevated ANP levels may be a marker of the
risk of ventricular dilatation and thus increased mortality.
Dor et al reported a significant increase in ventricular vol-
umes in all subsets of patients one year after operation, com-
pared to the early postoperative period [10].

Compared to Nt-proANP, the Nt-proBNP did not in-
crease significantly. This was in consonance with other stud-
ies where LVEDP correlated significantly with ANP but not
BNP levels [15]. Plasma concentration of BNP however,
rose in patients with symptomatic left ventricular systolic
dysfunction [16, 17]. There was a strong correlation between
BNP and left ventricular ejection fraction. It is possible that
changes in left ventricular ejection fraction are better re-
lected by BNP, while LVEDP is better mirrored by ANP.

Other neurohormones did not change significantly. A posi-
tive correlation was found between the preoperative levels of
circulating arginine vasopressin and the postoperative
improvement of stroke volume (r = 0.80; p = 0.02). This could
be a chance finding or it possibly could reflect the fact that
neuroendocrine activation increases with the increase in left
ventricular dysfunction [18], and that the patients who ben-
fit most from endoaneurysmorrhaphy are those with more
severe preoperative left ventricular compromise [10]. We
also observed a significant rise in stroke volume in only those

Table 1. Haemodynamic Data

<table>
<thead>
<tr>
<th></th>
<th>Preoperative</th>
<th>Postoperative</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>LVEF(%)</td>
<td>31.7 ± 4.3</td>
<td>48.2 ± 4.4</td>
<td>0.001*</td>
</tr>
<tr>
<td>ESV (ml)</td>
<td>130 ± 18</td>
<td>84 ± 16</td>
<td>0.02*</td>
</tr>
<tr>
<td>EDV (ml)</td>
<td>190 ± 22</td>
<td>154 ± 19</td>
<td>0.12</td>
</tr>
<tr>
<td>SV (ml)</td>
<td>66 ± 11</td>
<td>67 ± 5</td>
<td>0.97</td>
</tr>
<tr>
<td>LVEPSP mm Hg</td>
<td>107 ± 9</td>
<td>109 ± 4</td>
<td>0.86</td>
</tr>
<tr>
<td>LVEDP mm Hg</td>
<td>11.3 ± 2.4</td>
<td>19.1 ± 3.5</td>
<td>0.03*</td>
</tr>
<tr>
<td>HR (beats/min)</td>
<td>76 ± 5</td>
<td>89 ± 7</td>
<td>0.06</td>
</tr>
</tbody>
</table>

LVEF = left ventricular ejection fraction; ESV = end systolic volume; EDV = end diastolic volume; SV = stroke volume; LVEPSP = left ventricular end systolic pressure; LVEDP = left ventricular end diastolic pressure; HR = heart rate, * = statistical significance

Figure 1. Scattergram illustrating the relationship between postoperative left ventricular end-diastolic pressure (LVEDP) and N-terminal proatrial natriuretic peptide (Nt-proANP) plasma concentration.
patients who had a low pre-operative stroke volume (< 70 ml). It therefore transpires that if the observations are validated in a larger study, preoperative arginine vasopressin levels may be used as markers of post-operative improvement.

There are certain limitations of the study. Besides small cohort size and short follow up, there is absence of a control group with myocardial revascularisation but no EAR. Cardioactive drugs, which could have significant influence on neurohumoral status, were continued throughout the study period. Finally, follow up does not include clinical status.

In conclusion, there appears to be a discordance in left ventricular pump functions after endoaneurysmorrhaphy early postoperatively. An improvement in systolic performance is accompanied by a worsening of diastolic function. This is further demonstrated by an increase in Nt-proANP, a bad prognosticator. The observations are preliminary and need further validation.

Acknowledgement

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References

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