Abstract. – Objectives: During extracorporeal circulation (ECC) there is a great hemodynamic stress with possible impact on the microcirculation, including cochlear one. Previous studies have evaluated the effect of ECC on inner ear with contrasting results. The aim of this study is to evaluate possible modifications of the outer hair cells (OHC) function after open heart surgery (OHS) under ECC with transient evoked (TEOAEs) and distortion product otoacoustic emissions (DPOAEs).

Methods: Ten patients (5 F and 5 M), undergoing OHS with ECC, were subjected to an audiological assessment pre- and postoperatively. We compared the pre-operative and post-operative mean auditory thresholds, mean TEOAEs reproducibility and amplitude, and mean DPOAEs amplitude. Student’s t-test was used to compare different values.

Results: No significant differences were found between pre- and post-operative audiological assessment both in hearing level and in otoacoustic emissions.

Conclusion: OHC function seems to be not affected by hemodynamic stress induced by ECC. Further studies on a larger scale will be necessary to confirm our preliminary data.

Key Words:
Hearing loss, Otoacoustic emissions, Cardiopulmonary bypass, CPB complications, Neurologic injury.

Introduction

The inner ear is irrigated by a fine microcirculation supplied from a terminal branch of the basilar artery. Minimal alterations in labyrinthine microcirculation can lead to a significant cochlear dysfunction. The anatomical and functional integrity of cochlea, specifically of outer hair cells (OHCs), can be evaluated with otoacoustic emissions (OAEs). OAEs are low-intensity sounds emitted by OHCs, recorded in the external ear canal by a microphone positioned in an ear probe, in response to an auditory stimulation (transient evoked otoacoustic emissions and distortion product otoacoustic emissions) or spontaneously (spontaneous otoacoustic emissions).

Many stress factors have been reported to alter the OHCs function, among these hypotension and ischemia. Extracorporeal circulation (ECC) is a perfusion procedure required for cardiac surgery using a cardiopulmonary bypass circuit, in which the risk of hypotension and ischemia is higher, because it determines a modification of physiological blood flow from pulsating to continuous and can generate microemboli. Furthermore, surgery under ECC is associated to hypothermia, another condition potentially harmful reported in literature.

The incidence of unilateral sensorineural hearing loss after open heart surgery performed with extracorporeal circulation (ECC) is around 0.1%, higher than the general population (0.02%). Cardiac surgery interventions with ECC should determine worse pure tone thresholds than interventions without ECC ("off-pump" surgery).

The aim of this study is to examine possible changes of the OHCs function in the immediate post-operative time after heart surgery under ECC with transient evoked otoacoustic emissions (TEOAEs) and distortion product otoacoustic emissions (DPOAEs).

Materials and Methods

Patients

Sixteen patients undergoing cardiosurgery interventions (myocardial coronary artery bypass
and valvular surgery) with ECC were studied from September 2008 to May 2009 at the University of Campus Bio-Medico, Rome (Italy). The sample consisted of 16 patients, 7 women and 9 men, with a mean age of 63 years (ranged 56-68 years). All patients were subjected to a clinical otological examination, a pure tone audiogram, impedance audiometry and otoacoustic emissions the day before surgery (pre-operative phase) and 72 hours after surgery (post-operative phase).

We exclude from the study patients with clinical history of use of drugs with verified ototoxicity, chronic otitis media, labirintitis, meningitis, noise exposure; externa ear patologies; abnormal tympanometry. Since TEOAEs are detectable only with normal hearing or in patients with a pure tone threshold inferior to 30 decibel (dB) SPL and with an air-bone gap of <5 dB at any frequencies, 3 patients were excluded from the study due to a pure tone threshold >30 dB SPL.

Furthermore, we excluded 1 patient because of history of noise exposure, another patient was not submitted to intervention and another one could not undergo post-operative phase analysis. Finally, 10 patients, 5 women and 5 men, with a mean age of 62.8 years (ranged 56-68 years) were included in the study.

The study protocol was approved by the Research Ethics Committee at our institution and each patient signed a written informed consent.

**Audiological Assessment**

The audiometric tests conformed to the specification in ISO 8253. Pure-tone average (PTA) and air-bone gaps (ABG) were calculated for each audiogram.

The analysis of otoacoustic emissions was performed through an ILO96 Otodinamycs analyzer (V5 ILO OAE Research, Otodynamics, London, United Kingdom). The observed TEOAEs were the ILO88 elaborated by Kemp. The stimuli were represented as clicks of 80 μs with a frequency of 50 Hz. These were measured as groups of 4 clicks that consisted of 3 clicks with identical polarity and amplitude, with the fourth click of greater intensity and inverse polarity. The level of stimulus was approximately of 80 dB SPL; the response was registered between 2.5 to 20.5 ms after the stimulation. A total of 260 sweeps was averaged for a complete response. The response analysis included the parameters of wave reproducibility and the signal to noise ratio. TEOAEs were considered to be present if wave reproducibility was ≥60% and amplitude of the signal to noise ratio ≥3 dB.

DPOAEs were recorded as “Dp-gram”. Two equilevel (L1 = L2 = 70 dB SPL) primary tones of frequencies f1 and f2 were presented simultaneously with a frequency ratio (f2:f1) fixed at 1:224. Dpgram was obtained as function of F2 frequency, ranging from 1001 to 6299 Hz in 1/4 octave steps. DP-grams have not been extended at F2 frequencies lower than 1 kHz, since the excessive background noise contaminate the DPOAE measurements. The cubic distortion product 2f1-f2, elicited in response to a stationary stimulus amplitude, was evaluated. DPOAE was considered to be present if 2f1-f2 was ≥ dB SPL. The amplitude of response of distortion product 2f1-f2 in relation to background noise (in dB SPL) was used for purposes of statistical analyses.

**Surgery**

All surgical interventions were performed with ECC by the same team of surgeons and anaesthetists under general anesthesia.

General anesthesia was induced intravenously with 4 mg of midazolam, 0.6 mg of fentanyl citrate and 8-10 mg of vecuronium. Anesthesia was maintained with propofol 10 ml/h iv injection and a mixture of sevoflurane 2%, oxygen and air. Cardioplegia consisted of St. Thomas’ II cardioplegic solution. During each intervention the nasopharyngeal temperature reached 32°C. ECC was provided by a centrifugal pump (Biomedicus; Medtronic, Eden Prairie, MN, USA), SARNs 3M pumps, a Stockert heat exchanger, a heparin-coated membrane oxygenator (Trillium Affinity; Medtronic) and venous and arterial tubing (Medtronic). No ototoxic drugs were used during the perioperative period.

Six patients were submitted to coronary bypass intervention, two to aortic valve substitution, two to mitral valve substitution. Data of patients, type of surgery, cross-clamp time, cardiopulmonary bypass time, arterial mean pressure during cardiopulmonary bypass are shown in Table I.

**Statistical Analysis**

The statistical analysis was performed using the statistical Package for Social Sciences Software (SPSS 10.0 for windows; SPSS Inc., Chicago, IL, USA). We compared the pre-operative and post-operative mean auditory thresholds, average TEOAEs reproducibility and amplitude.
and average DPOAEs amplitude. Data are shown as means and standard deviations. Student’s paired \( t \)-test was used to compare different values. Our criterion for statistical significance was set at \( p \)-values of less than 0.05 (two-tailed).

### Results

Cross-clamp time ranged from 37 to 60 min (mean=54.4 min), cardiopulmonary bypass time ranged from 65 to 93 min (mean=82 min) and arterial mean pressure during bypass ranged from 53 to 77.5 mmHg (mean=68.34 mmHg).

None of the patients in the postoperative period reported otological symptoms (tinnitus, hearing loss, dizziness).

Comparing pre- and post-operative bone conduction pure tone average, we did not find any statistically significant difference \( (p>0.05) \).

The average reproducibility of TEOAEs was 62.3\% ± 19.2\% in pre-operative phase and 63.6\% ± 18.17\% in post-operative phase. The average amplitude of the signal to noise ratio was 3.36 ± 1.54 dB SPL in pre-operative phase and 3.61 ± 1.46 dB SPL in post-operative phase. No significant difference was found in the TEOAE parameters pre- and post-operatively (reproducibility: \( p=0.74 \); amplitude: \( p=0.4 \)).

The comparison of the pre- and post-operative values of the DPOAE amplitude levels (Table II), for each F2 frequency analyzed (1001 Hz to 6299 Hz), showed a not statistically significant difference \( (p>0.05) \) of the amplitude of the responses in the post-operative phase.

### Table I. Data of patients.

<table>
<thead>
<tr>
<th>Patient</th>
<th>Age (ys)</th>
<th>Sex (M/F)</th>
<th>Type of surgery</th>
<th>Cross-clamp time (min)</th>
<th>Bypass time (min)</th>
<th>Pressure during bypass (mmHg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>P L</td>
<td>58</td>
<td>M</td>
<td>Coronary bypass</td>
<td>37</td>
<td>78</td>
<td>73.75</td>
</tr>
<tr>
<td>T F</td>
<td>63</td>
<td>F</td>
<td>Coronary bypass</td>
<td>51</td>
<td>90</td>
<td>75</td>
</tr>
<tr>
<td>C G</td>
<td>68</td>
<td>F</td>
<td>Coronary bypass</td>
<td>59</td>
<td>68</td>
<td>70.15</td>
</tr>
<tr>
<td>C L</td>
<td>61</td>
<td>M</td>
<td>Coronary bypass</td>
<td>59</td>
<td>81</td>
<td>68.75</td>
</tr>
<tr>
<td>G R</td>
<td>56</td>
<td>F</td>
<td>Aortic valve substitution</td>
<td>57</td>
<td>90</td>
<td>70.2</td>
</tr>
<tr>
<td>P A</td>
<td>67</td>
<td>F</td>
<td>Aortic valve substitution</td>
<td>58</td>
<td>93</td>
<td>75</td>
</tr>
<tr>
<td>LE</td>
<td>66</td>
<td>M</td>
<td>Coronary bypass</td>
<td>45</td>
<td>65</td>
<td>77.5</td>
</tr>
<tr>
<td>C P</td>
<td>59</td>
<td>M</td>
<td>Coronary bypass</td>
<td>60</td>
<td>80</td>
<td>55</td>
</tr>
<tr>
<td>C P</td>
<td>65</td>
<td>M</td>
<td>Mitral valve substitution</td>
<td>58</td>
<td>90</td>
<td>53</td>
</tr>
<tr>
<td>S M</td>
<td>65</td>
<td>F</td>
<td>Mitral valve substitution</td>
<td>60</td>
<td>85</td>
<td>65</td>
</tr>
</tbody>
</table>

### Table II. DPOAE amplitude levels (in dB SPL) for each frequency.

<table>
<thead>
<tr>
<th>DP frequencies</th>
<th>Average pre</th>
<th>Average post</th>
<th>Standard deviation pre</th>
<th>Standard deviation post</th>
<th>( t )-test</th>
</tr>
</thead>
<tbody>
<tr>
<td>1001 Hz</td>
<td>14.45</td>
<td>16.97</td>
<td>8.85</td>
<td>1.3</td>
<td>0.41</td>
</tr>
<tr>
<td>1184 Hz</td>
<td>17.16</td>
<td>13.38</td>
<td>12.35</td>
<td>9.74</td>
<td>0.29</td>
</tr>
<tr>
<td>1416 Hz</td>
<td>16.49</td>
<td>13.67</td>
<td>12.31</td>
<td>9.57</td>
<td>0.36</td>
</tr>
<tr>
<td>1685 Hz</td>
<td>16.3</td>
<td>19.03</td>
<td>8.28</td>
<td>12.1</td>
<td>0.38</td>
</tr>
<tr>
<td>2002 Hz</td>
<td>14.75</td>
<td>18.34</td>
<td>10.29</td>
<td>12.42</td>
<td>0.22</td>
</tr>
<tr>
<td>2380 Hz</td>
<td>19.35</td>
<td>15.11</td>
<td>11.19</td>
<td>9.42</td>
<td>0.16</td>
</tr>
<tr>
<td>2832 Hz</td>
<td>18.18</td>
<td>15.16</td>
<td>11.33</td>
<td>9.67</td>
<td>0.3</td>
</tr>
<tr>
<td>3369 Hz</td>
<td>19.79</td>
<td>15.3</td>
<td>12.94</td>
<td>10.32</td>
<td>0.18</td>
</tr>
<tr>
<td>4004 Hz</td>
<td>15.97</td>
<td>19.51</td>
<td>13.2</td>
<td>13.71</td>
<td>0.41</td>
</tr>
<tr>
<td>4761 Hz</td>
<td>18.72</td>
<td>17.25</td>
<td>13.99</td>
<td>10.74</td>
<td>0.73</td>
</tr>
<tr>
<td>5652 Hz</td>
<td>15.17</td>
<td>17.49</td>
<td>9.12</td>
<td>10.5</td>
<td>0.47</td>
</tr>
<tr>
<td>6299 Hz</td>
<td>15.04</td>
<td>13.02</td>
<td>10.45</td>
<td>8.95</td>
<td>0.52</td>
</tr>
</tbody>
</table>
Conclusion

The outer hairy cells (OHCs) are the contractile structures of the inner ear, responsible for non-linear cochlear activity, that can be recorded with OAEs, considered a sensitive test for monitoring preclinical alterations of OHCs function. The data show no significant difference of the amplitude of the TEOAEs and DPOAEs in the post-operative phase, that provides evidence for a structural and functional integrity of the OHCs. Different pathogenetic mechanisms have been proposed to explain sensorineural hearing loss after ECC including endothelial damage, variations of cerebrospinal fluid (CSF) pressure, anesthetics, hypoperfusion-hypotension, hypercoagulability, microembolism, inflammatory stimuli induced by ECC, vasospasm, continuous blood flow. Cardiac surgery with ECC is a procedure that impairs the normal function of various organs, particularly central nervous system (CNS). The main pathophysiologic mechanisms of ischemic injury of CNS seem to be hypoperfusion and microembolism. The possible sources of microemboli during ECC include the bubble oxygenators, cardiotomy reservoir, loose purse-string sutures, ruptured atherosclerotic debris, hemolyzed red cells, platelet-leukocyte aggregates and foreign materials. The presence of microemboli during ECC has been demonstrated in CNS by transcranial Doppler ultrasonography and in retinal microcirculation by fluorescein angiography. A similar mechanism could be hypothesized in inner ear microcirculation, causing a cochlear damage involving the outer hair cells, the most fragile structure of the cochlea.

We believe that these risk factors may have not been sufficiently intense in this sample to induce a damage of cochlea or that the cochlear mechanisms of recovery have been able to effect an intracellular “self-repair” of partially damaged auditory hair cells. Many studies increase the evidence of “self-repair” processing of the inner ear sensory epithelium after injury.

In conclusion, it seems that the ECC does not necessarily determine a change of outer hair cells activity and that the cases of hearing loss reported by many Authors are due to complications of heart surgery under general anesthesia rather than an effect intrinsic to cardiopulmonary bypass circuit.

Ness et al. did not find any causal relationship between sensorineural hearing loss and aortocoronary bypass surgery in a sample of 145 patients, supporting that hearing loss following bypass may be attributed to the ototoxic therapy.

Iriz et al. showed the absence of statistically significant DPOAE shifts in 21 patients undergoing coronary artery bypass grafting, concluding that hearing loss after open heart surgery may be due to general anesthesia.

Considering the high sensitivity of the OAEs in detecting the smallest changes in the cochlea, our data confirm, despite the restricted sample size, the extraordinary potential of the cochlea and low probability of cochlear damage after cardiac surgery.

Certainly, it is necessary to perform this analysis on a greater sample of patients so as to inquire the infrequent cases of sensorineural hearing loss, valuing in each patient the possible variations of otoacoustic emissions and the clinical conditions or complications which produce these change of OHCs activity, performing a long term audiological follow-up to evaluate possible progressive damage of cochlea.

However, we suggest that the otoacoustic emissions could have an important role in perioperative monitoring when a surgical intervention is suspected to be potentially harmful to hearing.

References


