SUMMARY

Rapid developments in cardiac implantable electronic device (CIED) technology leading to implantation of various types of PM/CRT/ICDs combined with extended indications for CIED therapy and changes in patient profile are the underlying cause of the rise in CIED implantation. Approximately 1.2 to 1.4 million patients receive CIED annually worldwide. Fast increases in life expectancy, the patients having multiple diseases and the increasing rates of CIED implantation increase also the rates of permanent pacing failures and complications. Transvenous lead extraction (TLE) has been used as a first-line treatment for CIED-related complications for over 30 years. According to the European Heart Rhythm Association (EHRA) reports approximately 9000 lead extractions are performed annually in over 350 centers in Europe. Lead removal may be indicated for infectious complications such as lead-related endocarditis, sepsis, pocket infection. The most frequent non-infectious indications include mechanical lead damage with an open circuit, lead dysfunction due to loss of contact between the lead tip and the endocardium or lead penetration through the myocardial wall, redundant dysfunctional leads, anomalous course of the lead in the cardiovascular system or lead interference with tricuspid valve apparatus that significantly impairs valve function. Less frequently CIEDs are removed due to the necessity of performing magnetic resonance imaging (MRI) in patients with non MRI-conditional devices, radiation therapy for chest wall neoplasms, and regaining vascular access when thoracic veins are obstructed.

The lead is most frequently dissected away from the fibrous tissue in its intravascular and intracardiac segment using mechanical dilator sheaths, less frequently laser energy. Data from a number of studies suggest that TLE is highly effective and associated with low risk of major complications, which is 0.4-4.0% and 0.00-1.86%, respectively. Positive outcomes depend on the operator's experience and training as well as high performance standards. The 2017 Heart Rhythm Society (HRS) and the 2018 European Heart Rhythm Association (EHRA) recommend using continuous transesophageal echocardiography (TEE) monitoring or intracardiac echocardiography (ICE) during TLE to improve patient safety.

This study evaluated the usefulness of continuous TEE monitoring in patients undergoing TLE to prevent the occurrence of complications through identification of prodromal phenomena which are not visible in fluoroscopy. Furthermore, the study confirmed the role of TEE in the rapid diagnosis of complications, especially of hemorrhagic character and a possibility of excluding the presence of complications in case of transient patient instability due to a reduction in the right ventricular lumen during TLE. TEE monitoring was also found to

optimize and improve patient safety during TLE. The study is based on the clinical material from two largest TLE centers in Poland performing from 250 to 270 procedures annually.

Methods. This study analysed the medical documentation related to 1026 TLE procedures performed in 2015-2019 at the tertiary referral center in Zamość. A total of 936 procedures under TEE guidance were selected for further analysis. In the latter subgroup all phenomena observed during TEE were analysed in the consecutive phases of TLE.

To achieve the study aim II, a control group was formed consisting of 2106 TLE procedures without TEE monitoring performed at another tertiary referral center in Lublin between 2006 and 2015. Two groups were compared: 2106 patients with echocardiographic evaluation before and after TLE and 1079 patients with continuous TEE monitoring during TLE between June 2015 and January 2020. The clinical data, device type, complexity of TLE, occurrence of major complications and long-term survival were also compared.

To estimate the safety and efficacy of the procedure the SAFeTY-TLE prognostic score was used to predict the occurrence of major complications [II: 15]. All TLE procedures at both tertiary referral centers were performed by the same experienced operator. Mechanical dilator systems were used such as polypropylene Byrd dilators (Cook® Medical, USA), using whenever possible extracted lead venous approach, most frequently via the subclavian vein. If necessary, mechanical catheters with a manual drive (Evolution, Cook® Medical, USA; TightRail, Spectranetix, USA), or specialized sheaths such as lasso and basket catheters were applied. The indications for TLE and type of periprocedural complications were defined according to the expert consensus of the 2017 Heart Rhythm Society (HRS) and the 2018 European Heart Rhythm Association (EHRA) [I: 8, 9: II: 13, 14].

TEE was performed using 3D/4D probes. The acquired images were archived and then post-processed. TEE monitoring was carried out in three phases as proposed by the HRS 2017 and EHRA 2018 experts [I: 8, 9; II: 13, 14] encompassing pre-, intra- and post-procedure evaluation in patients undergoing TLE. Standard TEE projections were used and individual modifications for best imaging of the evaluated structures. In the pre-procedure phase information about lead position verified by fluoroscopy, the degree of fibrosis binding the lead to venous and cardiac walls and lead-to-lead adhesions was documented. Additional masses on the leads, tricuspid valve function and the separation of pericardial layers were also evaluated. In the intra-procedure phase, during lead extraction, pulling on the heart structures, reduction in right ventricular lumen and the effect of these phenomena on the hemodynamic state of the patient were assessed. Furthermore, pulling on the other lead, dislodgement of fibrous tissue fragments or vegetations attached to the leads and the separation of pericardial layers were checked during

lead removal. In the post-procedure phase, tricuspid valve function, the presence of remnants after the extraction (lead tips, vegetations, residual fibrosis), pericardial effusion and the rate of fluid accumulation were evaluated. Additionally, TEE after TLE was used for visualization of the coronary sinus orifice during implantation of left ventricular leads, and also for evaluation of the position of right ventricular leads coursing the tricuspid valve to ensure the mobility of valve leaflets.

In statistical analysis, quantitative data were expressed as means and standard deviations, whereas qualitative data as numbers/counts and the percentage. The Shapiro-Wilk test was used to check for normality. The nonparametric Mann-Whitney U test was used to compare differences between groups. Quantitative data were expressed as the number and percentage of cases. The Chi2 test with Yates correction was applied for drawing a comparison. The Kaplan-Meier method was used to construct survival curves and evaluate the effect of TEE monitoring on long-term outcomes after TLE. The log-rank test was used to assess differences in longevity. A p-value less than 0.05 was considered statistically significant. Statistical analysis was performed using Statistica v. 13.3.

Results. Among the 936 patients undergoing TLE with TEE monitoring 151 (16.1%) individuals had lead-related infective endocarditis (LRIE) and 58 (6.2%) pocket infection. The remaining 727 (77.6%) noninfectious indications included lead dysfunction, the necessity of regaining vascular access, lead-dependent tricuspid valve dysfunction, the need for radiation therapy or MRI in patients non MRI-conditional devices. The mean age of the study group was 67.1 ±14.4 years. On average, 1.66 ±0.75 leads were extracted in one patient, with the mean implant duration being 115.8 ±77.6 months. During TLE there were 18 (1.9%) major complications including 12 (1.3%) cases of pericardial bleeding, 6 (0.6%) cases of significant permanent tricuspid valve damage and one (0.1%) case of pleural hemorrhage. Eleven (1.1%) patients required surgical intervention. There were no periprocedural deaths.

In the pre-procedure phase the most common TEE finding was lead adhesion to the right ventricular wall in 106 (11,3%) cases and to the tricuspid apparatus in 90 (9.6%) cases. The occurrence of lead adherence to the superior vena cava and the right atrium was similar, i.e. 56 (5.9%) and 65 (6.9%) cases, respectively. Lead-to-lead adhesions were detected in 172 (18.4%) patients. Excessive lead loops were found in 181 (19.3%) cases, most frequently in the right atrium 138 (14.7%) patients. The lead tip in the position indicating myocardial wall penetration or perforation was demonstrated in 151 (16.1%) cases. In contrast to fluoroscopy, echocardiography enabled a more precise detection of rare atypical lead positions in the intermediate cardiac vein, aortic bulb and foramen ovale. Lead thickening and

hyperechogenicity corresponding to fibrous encapsulation was detected in 160 (17.1%) cases. Among the infectious patients vegetations were found in 119 (12.7%) individuals. The vegetations were mostly small (<2 cm); there were 10 large vegetations 2.1-3.0 cm (1.1%), and 14 vegetations >3 cm (1.5%) in size. Lead-dependent tricuspid dysfunction (LDTD) was diagnosed in 60 (6.4%) patients.

In the intra-procedure phase continuous TEE monitoring revealed pulling on the atrial wall during 380 (40.6%) procedures, pulling on the tricuspid leaflet/ring in 78 (8.3%) patients, right ventricular wall in 235 (25.1%), simultaneous pulling on the other lead in 104 (11.1%) cases. In 51 cases (5.4%) bacterial vegetations attached to the leads were freed up. Residual fibrosis (encapsulations, "ghosts") after lead extraction was observed in 111 (11.8%) procedures. Despite the detection of migrating vegetations or fibrotic fragments there were no clinical consequences. In 50 (5.3%) cases TEE demonstrated broken lead fragments which were successfully removed. In 4 (0.4%) cases a fragment of silicone insulation was left behind, which was visible only on echocardiography. The removal under TEE guidance was successful in each case. Self-limiting pericardial effusion, without significant clinical consequences, occurred in 22 (2.2%) cases. In 11 out of 12 (1.2%) patients acute cardiac tamponade was due to right atrial wall damage. This study analysed changes in systolic blood pressure taking into account the moment of mechanical traction applied to the lead. Hemodynamic instability occurred during 20% of procedures, and the mean fall in systolic blood pressure was 20.8 mmHg ±14.5. Pulling on the right ventricle with a significant reduction in its lumen was responsible for hemodynamic instability in 70% of cases.

In the post-procedure phase TEE detected fibrous remnants in 310 (33.2%) cases, most frequently in the right atrium (183; 47.2%) and in the superior vena cava (98; 25.3%). In the subgroup with infectious indications vegetation remnants 2.57±1.7 mm in size were found in 69 (7.3%) cases. Significant damage to the valve apparatus was detected in 33 (3.5%) TLE procedures, including 6 (0.6%) with permanent valve damage that caused severe regurgitation requiring repair, on an urgent basis in one case. It is also worth pointing out that there was a significant improvement of tricuspid function after TLE in 12 (1.3%) cases.

Data from another 143 TLE procedures under TEE guidance added to the data from 936 patients were compared with data from 2106 procedures without intra-procedure TEE imaging. The expected rate of complications in the two study subgroups was calculated using the SAFeTY-TLE score. Patients undergoing "monitored" TLE were generally older, more frequently had accompanying diseases (*Charlson comorbidity index* 4.97 ±3.75 vs. 4.43 ±3.53; $p<0.001$), low mean hemoglobin concentrations and renal failure as compared with patients undergoing "non-

monitored" TLE. Arterial hypertension was more frequent among the "non-monitored" patients (60.77 vs. 53.01; p<0.001). Age of the patients at first pacemaker implantation was similar (58.09 ±15.81 vs. 57.34 ±17.62; p=0.558), whereas the "monitored" patients were older when undergoing TLE (67.41 ±14.23 vs. 64.84 ±16.22; p<0.001) and they had mostly noninfectious indications for lead removal (77.94% vs. 60.35%; p<0.001). In the "non-monitored" group the main indications were lead-related infective endocarditis (27.63% vs. 15.47%; p<0.001) and pocket infection (12.01% vs. 6.58%; p<0.001). The number of leads in the CIED system was similar. The "monitored" group was characterized by having older leads (112.66 ±75.95 months vs. 90.80 ±69.95; p<0.001), ICD leads or left ventricular leads (35.12% vs. 30.00%; p<0.01), and fewer abandoned leads (0.08 ±0.28 vs. 0.13 ±0.34; p<0.05).

The two groups did not differ in the number of extracted leads in one patient (1.63±0.71 vs. 1.66±0.76; p=0.47, on average). The "monitored" group differed from the "non-monitored" one by older age of the extracted leads (15.46 ±13.96 vs. 11.87 ±11.00 years; p<0.001), more frequent removal of ICD leads (31.60% vs. 25.30%; p<0.001), less frequent extraction of left ventricular leads (11.30% vs. 14.00, p<0.05) and abandoned leads (8.80% vs. 15.52%; p<0.001). In the "monitored" group technical difficulties were more common (23.81% vs. 15.90%; p<0.001), second-line equipment was also used more frequently (6.95% vs. 5.12%; p<0.05). The duration of the procedure was significantly longer in the "monitored" group. Complete procedural success was significantly higher in the "monitored" group (97.68% vs. 95.44%, p<0.01), whereas clinical success was similar in the two groups. In the periprocedural period no deaths occurred in the "monitored" group as compared with 6 deaths (0.28%) in the "non-monitored" group (p=0.18). Mortality rates at 6 and 12 months after TLE were similar.

The total risk score on the SAFeTY-TLE scale was higher in the "monitored" group (6.14 ±4.39 vs. 5.59 ±4.12; p= 0.004). A significantly higher risk of major complications in this subgroup was related to older age of the extracted leads (≥ 16.5 years) and lower hemoglobin concentrations (< 11.5 g/dl; p<0.001). As expected, there was also a significantly higher risk of venous and cardiac perforations: 1.89 (95%CI: 1.66-2.13) vs. 1.63 (95%CI: 1.47-1.78), p=0.002. The SAFeTY-TLE score predicted 21 perforations of the superior vena cava, right atrium and right ventricle during TLE in the "monitored" group and 34 events in the "non-monitored" group. The score of major complications was similar in the "monitored" and "non-monitored" groups, i.e. 21 (1.94 %) vs. 39 (1.85 %) events. Detailed analysis showed a similar rate of pericardial or pleural hemorrhage and tricuspid damage in both groups, however in the "monitored" group there were 6 fewer bleeding incidents than predicted on the SAFeTY-TLE

scale, which corresponded to a risk reduction of 28.57% ($p<0.05$). In the "non-monitored" group there were 33 analogical major complications as compared with the predicted 34.

Recapitulation. The results of the present study for the first time confirmed the efficacy of transvenous lead extraction and reduced risk of cardiac and venous damage during TLE procedures with TEE monitoring. Continuous TEE monitoring was also found to help achieve 100% periprocedural survival. It should be noted that TEE monitoring enables safe performance of much more difficult procedures in patients at high risk through anticipation of problems before they occur based on analysis of cardiac function in response to operator manipulations which are invisible on fluoroscopy. What is also important is that such an approach enables modification of the extraction technique and in some cases helps prevent the occurrence of complications. It appeared very important for the operator and further patient care to evaluate lead position and course, interrelationships between leads and anatomical heart structures, the presence of additional masses on the leads and their behaviour during lead extraction, tricuspid dysfunction, the presence and the rate of pericardial fluid accumulation, the underlying cause of hemodynamic instability and right heart function after lead extraction.

Conclusions

1. TEE monitoring of TLE can be divided into 4 phases: pre-procedure phase from the moment of probe placement to the beginning of lead dissection, intra-procedure phase, i.e. the moment of lead removal, post-procedure phase evaluating TLE efficacy/possible damage, and an optional phase 4, i.e. implantation of a new lead.
2. In the pre-procedure phase TEE performed under comfortable conditions both to the patient and the echocardiographer serves as a source of valuable information about possible difficulties which may affect the procedure technique.
3. The intra-procedure phase encompasses the monitoring of the very moment when the lead is being removed combined with echocardiographic imaging of pulling on the cardiac walls and observation of the right ventricular lumen to prevent systolic blood pressure from dropping. An important part of the phase is also echocardiographic evaluation of simultaneous pulling on the other lead in case of lead-to-lead adhesion, dissection and dislodgement of fibrous encapsulation fragments or vegetations. In case of cardiac wall damage and accumulation of fluid in the pericardial space, TEE helps the cardiac surgeon locate the site of damage after earlier inspection of the heart area with too much pulling during TLE. The phase enables also echocardiographic visualization of lead remnants and evaluation of the possibility of grasping and removing the pieces.

4. The post-procedure phase consists mainly of the evaluation of procedure efficacy and monitoring possible complications as well as qualification for further treatment. The phase includes also a comparative evaluation of tricuspid valve function, fibrous remnants and vegetation fragments.
5. In the phase of a new device implantation TEE monitoring may be useful for localization of the coronary sinus ostium, optimization of the lead position at the level of the tricuspid valve and the position of the lead tips.
6. A better understanding of the potential benefits of transesophageal echocardiographic monitoring during transvenous lead extraction is required among operators and echocardiographers to improve diagnosis and treatment of CIED-related complications.

Key words: transesophageal echocardiography, continuous intraprocedural monitoring, transvenous lead extraction