Short term results after an Alfieri repair in treatment of mitral regurgitation

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List of abbreviations

AF	Atrial fibrillation
ASD	Atrium septum defect
CABG	Coronary artery bypass grafting
CPB	Cardiopulmonary bypass
E-to-E	Edge-to-Edge
ERO	Effective regurgitant orifice
IDDM	Insulin dependant diabetes mellitus
LAA	Left atrial appendage
LVEF	Left ventricle ejection fraction
MR	Mitral regurgitation
MVR	Mitral valve ring
NIDDM	Non-insulin dependant diabetes mellitus
NYHA	New York Heart Association
REDCap	Research electronic data capture
SAM	Systolic anterior motion
SD	Standard deviation
TEE	Transoesophageal echocardiography
TTE	Transthoracic echocardiography

Abstract (dansk)

Baggrund og formål: Mitral insufficiens er den næst hyppigste hjerteklapsygdom og behandles oftest med mitralplastik, fx Alfieri-plastik, fremfor udskiftning af klappen. I dette studie undersøges de tidlige resultater efter Alfieri plastik ved Aalborg Universitets Hospital og sammenlignes med internationale studier.

Metode: Præ-, peri- og post-operative data blev indsamlet på patienter der havde fået en Alfieri plastik mellem september 2015 og september 2020. Data blev indsamlet fra Vestdansk Hjertedatabase og den elektroniske patient journal. En deskriptiv statistisk analyse blev lavet på data og præ- og postoperative resultater sammenlignet med en parret *t*-test blev ved et signifikansniveau på $p<0.05$. Mortalitetsraten blev beskrevet ud fra en Kaplan-Meier kurve.

Resultater: I alt 43 patienter blev inkluderet I dette studie og alle havde moderat (7.0%) eller svær (93.0%) mitralinsufficiens forårsaget af myxomatøs degeneration. Gennemsnitsalderen var 70.91 år (±7.82), og 22 patienter (51.2%) havde en NYHA score på I eller II. I alt 38 af patienterne (88.4%) havde komorbiditeter, oftest hypertension (60.5%) og atrieflimren (58.1%). Hos 23 patienter (53.5%) opstod postoperative komplikationer, oftest atrieflimren (32.6%). Kun 3 patienter (7.0%) havde rest-insufficiens og 38 patienter (90.5%) havde en NYHA score på I eller II postoperativt. To patienter blev reopererede (4.7%) og 6 patienter (14%) blev genindlagte indenfor 30 dage.

Konklusion: Den hjerte-lungekirurgiske afdeling ved Aalborg Universitetshospital, Danmark, har samme postoperative resultater som rapporteret i internationale studier, uanset den opererende kirurg. Dog vil en længere opfølgningsperiode, større studiepopulation og en femårs postoperativ klinisk opfølgning være eftertragtet, for mere præcise og sene resultater.

Abstract

Background and objectives: Mitral regurgitation (MR) is the second most common valve disease, and it is increasingly treated with mitral valve repair e.g., Alfieri repair in favour of valve replacement. In this study, short term results after an Alfieri repair from Aalborg University Hospital are compared with international results.

Methods: Pre-, peri- and post-operative data were collected from patients receiving an Alfieri repair between September 2015 and September 2020. Data were collected from the Western Danish Heart Registry and the electronic patient records. A descriptive statistical analysis was performed on all data and a paired *t*-test was used when comparing pre- and post-operative results with a level of significance at $p<0.05$. Mortality rate was determined using a Kaplan-Meier estimate.

Results: A total of 43 patients were included in this study and all had moderate (7.0%) to severe (93.0%) MR caused by myxomatous degeneration. Mean age was 70.91 years (± 7.82), 22 patients (51.2%) had a NYHA score of I or II and 38 patients (88.4%) had comorbidities, most commonly hypertension (60.5%) and AF (58.1%). A total of 53.5% had postoperative complications, most commonly AF (32.6%). Postoperatively only three patients (7.0%) had residual MR, and 90.5% had NYHA I or II. Freedom of reoperation was 95.3% and readmission within 30 days was 14.0%.

Conclusion: The short term results at the Department of Cardiothoracic Surgery, Aalborg University Hospital, Denmark, concerning mortality, occurrence of reoperation and readmission within 30 days after Alfieri repair is similar to those reported in international studies. However, a longer follow-up period, larger study population and five-year post-operative clinical follow-up, is to be desired for more precise and long-term results.

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1 Introduction

According to the Euro Heart Survey, moderate or severe mitral regurgitation (MR) is the second most common form of valvular abnormality with a need of surgical intervention(1). Furthermore, MR is increasingly prevalent in Europe(2). Approximately 1% of the danish population suffers from primary mitral valve regurgitation due to prolapse of the mitral valve leaflets (3) patients in Denmark suffer from cardiac valve disease(4) and the prevalence increases with age (1). The number of mitral valve surgeries is increasing in Denmark, as early diagnostics, better prognosis, and surgeries on elderly is becoming more common(5).

Mitral regurgitation pathology can be classified based on leaflet mobility using Carpentier's classification. Carpentier's type I describes normal leaflet motion with a dilated mitral annulus or leaflet perforation. Type II describes an excessive leaflet motion, which can be caused by chordal rupture, redundant chordae or papillary muscle rupture. Type II has two major phenotypes, 1) fibroelastic deficiency also called myxomatous degeneration, which is often caused by single chordal rupture or prolapse of an isolated scallop and 2) Barlow's disease, with thickened, redundant, elongated leaflets and chordae, with multiple scallops involved. Type III is caused by reduced leaflet mobility seen in rheumatic valve disease or myocardial ischemia, which can be subdivided into 1) IIIa with reduced mobility in diastole or both systole and diastole and 2) IIIb with reduced mobility only in the systole(1).

The primary treatment for MR has formerly been valve replacement (6). However, it has become evident that mitral valve repair is associated with lower risk of reoperation, valve infection, thromboembolism and a lower 30-day mortality rate, compared to mitral valve replacement (7,8). The most common repair techniques are resection of prolapsing segment(s), plication, folding-plasty, sliding leaftlet-plasty or an Alfieri repair (1).

The indications for surgical treatment of MR are based upon symptoms, the severity, end-systolic diameter, left ventricle ejection fraction (LVEF) and effective regurgitant orifice (ERO). In symptomatic patients, surgery is indicated when echocardiographic findings show a volume load on the left ventricle. In asymptomatic patients the indications for surgery are 1) an end-systolic diameter >4.5 cm and/or an affected LVEF of 30-60% or 2) an ERO >40 mm^2. Chronic MR can ultimately result in irreversible cardiac failure. Acute MR is always an indication for surgery as it can result in acute cardiac failure and pulmonary oedema (5).

The Alfieri repair was introduced in 1991 as an alternative to valve replacement when treating MR of Carpentier's type II (9). The Alfieri repair offers a functional repair, rather than an anatomical repair and reduces the surgical trauma performed in valve replacement, seemingly reducing the post-operative complications (10–13). A study by Raman et. al. showed a lower risk of complications such as bleeding, ischemia, and reoperation, when using the Alfieri repair compared to a mitral valve replacement (14). Furthermore, a study by De Bonis et. al. (2012) showed no in hospital deaths, a survival rate of 86.9%, freedom of reoperation of 89.6%, and 86.4% had mild or moderate MR (10) after a 14-year follow-up, indicating promising long-term results.

Indications for an Alfieri repair are: 1) MR of Carpentier's type II, 2) functional MR, 3) systolic anterior motion (SAM), 4) complex congenital atrioventricular valve incompetence and 5) suboptimal conventional mitral valve repair. Patients with a heavily calcified mitral annulus, no localised regurgitant jet, rheumatic MR, small mitral valve area or multiple mitral valve lesions are not suitable for an Alfieri repair, as this approach is related to worse outcome (6). Furthermore, patients with a LVEF of <30% are contraindicated for mitral valve surgery due to an expected postoperative reduction in LVEF of 5-10% (5).

At Aalborg University Hospital, mitral valve surgery is routinely performed through a midline sternotomy, but a right antero-lateral thoracotomy may also be used. Central cannulation is performed for cardiopulmonary bypass (CPB) and cross-clamp of the aorta with infusion of cardioplegia solution into the aortic root to achieve cardiac arrest, while running CPB. The mitral valve is exposed through a left atriotomy. Afterwards, the mechanism of MR is assessed through inspection and compared to the peri-operative echocardiographic findings. Mattress sutures are used to connect the two leaflets, creating a functional repair instead of an anatomical repair. The first stitch is used to symmetrically connect the two leaflets at the regurgitation site, without creating stenosis. A central Alfieri repair creates a double orifice when connecting A2 to P2, while commissural Alfieri repair creates a single orifice. Commissural repair can be done both posteromedial, when connecting A3 to P3 and anterolateral, when connecting A1 to P1 (figure 1) (9,15).

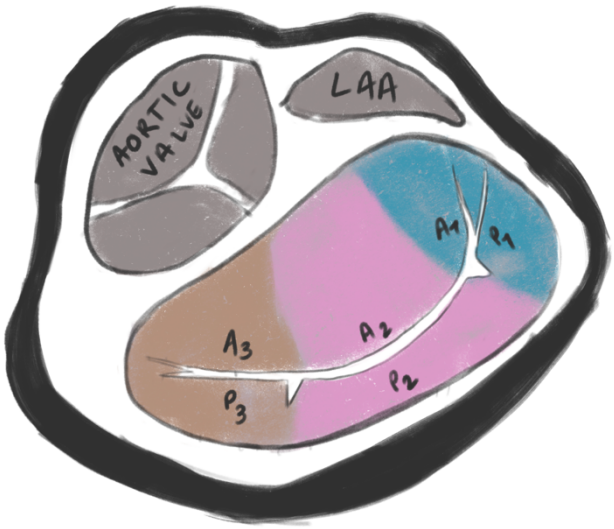

Figure 1 – Figure 1 shows the mitral valve and the two leaflets. The posterior leaflet is subdivided into three different sections, P1 (blue), P2 (pink), and P3 (brown). The anterior leaflet is also subdivided into three, A1 (blue), A2 (pink), and A3 (brown). LAA = left atrial appendage.

A rigid, semirigid or flexible prosthetic ring is implanted to increase coaptation surface of the leaflets, in order to reduce stress and stabilise the Alfieri repair (15), which has shown to be an advantage in multiple studies, in regards to durability and effectiveness of the repair, while reducing risk of post-operative complications (7,10,13,16–18). This approach is preferred if no contraindication is present, such as severe annular calcification or MR caused by SAM in hypertrophic obstructive cardiomyopathy. The size of the ring is determined through intertrigonal distance and the surface area of the anterior leaflet (15). The repair is evaluated through forceful saline injection into the left ventricle. During surgery, the Alfieri repair is evaluated through transoesophageal echocardiography (TEE) before the patient is leaving the operation room. A central Alfieri repair would show two diastolic flows (15,16,19).

Perioperative management was the same for all patients. Routine CPB settings are mean arterial pressure of ≥65 mmHg, flow rate of 2.2 to 2.4 L/min/m^2, mild hypothermia of 32-34^{o}C and haemoglobin ≥7.5 g/dL. For the CPB, oxygenated cold blood mixed with crystalloid in a 4:1 ratio was used (20,21).

At the Department of Thoracic Surgery at Aalborg University Hospital, Denmark, approximately 400-500 cardiac surgeries are performed yearly. During a 20-year period, a total of 662 patients have had

mitral valve surgery and of these 394 (59%) were mitral valve repairs. The first Alfieri repair was performed on April 25th 2000 and since then a total of 95 Alfieri repairs have been performed. In this study, we aim to compare the surgical outcome of the Alfieri repair at our low volume hospital, with high volume hospital internationally, in regard to mortality rate, risk of reoperation, and other post-operative complications such as residual MR and mitral valve stenosis.

We hypothesized that the surgical outcomes at Aalborg University Hospital are similar to those of international larger volume hospitals.

2 Methods

This quality assessment study is a retrospective study using prospective collected data from patient records and the Western Danish Heart Registry, which is a danish database collecting pre-, peri-, and post-operative information on all cardiac surgeries performed nationwide (22) The study was approved by the Hospital Administration and the Head of the Department of Cardiothoracic Surgery at Aalborg University Hospital, Denmark.

Patients who received an Alfieri repair were identified through the hospital's administrative record system. By law, we were only allowed to retrieve data regarding patients who had surgery less than five years prior to commencement of the study. We retrieved data of all patients who were recorded for having undergone an Alfieri repair at Aalborg University Hospital from September 2015 to September 2020. Patients with a MR classified as a Carpentier's type I or III, who received other types of mitral valve repair or received a mitral valve replacement were excluded from this study.

2.1 Data Sources

Pre-, peri- and postoperative data was collected from the patient records and the Western Denmark Heart Registry and data was compiled in Research Electronic Data Capture (REDCap®), which is a secure online tool for collecting and compiling patient sensitive data, hosted at the Region of Northern Jutland (23). The data was collected and reviewed twice independently by the two different authors, before data was transferred to IBM SPSS Statistics 27 (SPSS Inc. Chicago, IL, USA) for statistical analysis.

The following data were collected: comorbidities, previous cardiac surgeries, body mass index, preoperative plasma creatinine level, MR pathology, Euroscore II, pre- and post-operative New York Heart Association (NYHA) score pre and- postoperative LVEF, cross-clamp time, CPB time, concomitant procedures, ring type and size, type of Alfieri technique, re-hospitalisation and re-operation within 30 days of the Alfieri repair, mortality within five years of the Alfieri repair and postoperative complications such as atrial fibrillation (AF) diagnosed by telemetri/ECG, symptomatic myocardial ischemia, SAM, need for pacemaker in case of arrythmia, MR, mitral valve stenosis, stroke and acute renal insufficiency defined as a 50% increase in plasma was perceived as a complication, when a 50% increase in plasma creatinine withing seven days postoperatively (24).

Patients were monitored with telemetry and was along with clinical symptoms used to describe AF, need for pacemaker, and myocardial ischemia. Postoperative echocardiography was used to evaluate residual MR, mitral valve stenosis, but also SAM, in which, the anterior leaflet prolapsed into the ventricle during systole (25). All symptoms were defined as postoperative events when appearing within 30 days of surgery.

2.2 Echocardiography

Prior to the Alfieri repair, all patients underwent pre-operative TEE evaluation to determine the mechanism of MR using Carpentier's classification, LVEF and other possible cardiac pathologies (2).

As mentioned earlier, the mechanism of MR was re-evaluated using peri-operative TEE in case of concomitant procedures. Before patients were discharged, TEE or transthoracic echocardiography (TTE) was also used to evaluate the quality of the Alfieri repair and assess the presence of iatrogenic MR or mitral valve stenosis (19). Lastly, all patients received a three-month or one-year TEE/TTE follow-up. All LVEF simply described as normal was imputed as 60%, as normal LVEF is between 50-70% (5).

2.3 Statistical analysis

The collected data was transferred from REDcap® to the IBM SPSS Statistics 27 for analysis. A descriptive analysis was then performed on the data. Results such as LVEF, Euroscore II and age are presented as a mean (± standard deviation (SD)) value, while the remaining categorial data is presented as number of patients (percentage of patients). A paired *t*-test was performed when comparing continuous variables with a level of significance at $p<0.05$. A Shapiro-Wilk test was used to determine normality of the paired data. The survival proportion was determined using a Kaplan-Meier estimate following the methods of Goel et. al. (2010) (26).

3 Results

A total of 50 patients were recorded as having undergone Alfieri repair during the study period. However, seven patients were coded incorrectly and excluded leaving 43 patients for further analyses (*n*=43 patients). Table 1 shows the demographic data and preoperative characteristics of all patients. All cases of MR were caused by myxomatous degeneration and 40 (93.0%) patients had severe MR and only three (7.0%) had moderate MR. Mean age was 70.91 (± 7.82) years, 22 (51.2%) patients were NYHA I or II. Comorbidities were seen in 38 (88.4%) patients, with the most common comorbidities being AF (58.1%), hypertension (60.5%) and hypercholesterolemia (44.2%). A total of 6 (14.0%) patients had anterior leaflet prolapse, 17 (39.5%) had posterior leaflet prolapse and 20 (46.5%) had prolapse of both leaflets. The patients had a mean preoperative LVEF of 57.91 (± 10.87) %.

Table 1 – The table shows descriptive preoperative data for 43 patients.

Number of patients	43
Gender [male/female]	36/7
Age [years]	70.91 (± 7.82)
BMI [kg/m²]	24.29 (± 3.42)
Preoperative comorbidities	38 (88.4%)
Lung edema	1 (2.3%)
Renal insufficiency	0 (0.0%)
Aortic valve disease	1 (2.3%)
IDDM	2 (4.7%)
NIDDM	1 (2.3%)
Atrial fibrillation	25 (58.1%)
Hypertension	26 (60.5%)
Coronary disease	4 (9.3%)
Pacemaker	3 (7.0%)
Hypercholesterolemia	19 (44.2 %)

Previous Cardiac surgery	
CABG	1 (2.3%)
Aortic valve surgery	1 (2.3%)
Mitral valve surgery	0 (0.0%)
Other	1 (2.3%)
Pre operative LVEF [%]	57.91 (± 10.87)
Creatinin level [µmol/L]	90.05 (± 19.04)
NYHA	
NYHA I	4 (9.3%)
NYHA II	18 (41.9%)
NYHA III	16 (37.2%)
NYHA IV	5 (11.6%)
Euro-score [%] n=42	3.57 (± 3.16)
Operative priority	
Elective	38 (88.4%)
Urgent	4 (9.3%)
Emergent	1 (2.3%)
Leaflet	
Anterior	6 (14.0%)
Posterior	17 (39.5%)
Both	20 (46.5%)
Degree of MR	
Mild	0 (0.0%)
Moderate	3 (7.0%)
Severe	40 (93.0%)

Categorial data is presented as number of patients (% of the population). Remaining data is presented with a mean value (± SD). IDDM = insulin dependent diabetes mellitus. NIDDM = non-insulin dependent diabetes mellitus. CABG = coronary artery bypass grafting. Descriptive data can be seen in appendix 7.1.

Table 2 shows the operative data and associated procedures for all patients. At our hospital, a total of 42 operations (97.7%) were performed through midline sternotomy and one through thoracotomy (2.3%). The majority (72.1%) of patients received central repair, 10 (23.3%) received a posteromedial repair, while the remaining 2 (4.7%) patients received an anterolateral repair. Associated procedures were performed in 31 (83.7%) of the patients. Mean CPB time was 129.12 (± 37.44) minutes and mean cross-clamp time was 90.95 (± 31.8) minutes. A supportive mitral valve ring was inserted in 41 patients (95.3%). Two patients (4.7%) did not receive annuloplasty as contraindications was discovered perioperative due to annular calcification.

Table 2 – The table shows descriptive perioperative data for 43 patients.

Surgical technique	
Sternotomy	42 (97.7%)

Thoracotomy	1 (2.3%)
Annuloplasty ring	41 (95.3%)
Profile 3D Medtronic	17 (41.5%)
Liva Nova Memo 4D	15 (36.6%)
Duran	6 (14.6%)
Conture 3D Medtronic	3 (7.3%)
Ring size [mm]	37.95 (± 4.22)
Perfusion time [minutes]	129.12 (± 37.44)
Clamp time [minutes]	90.95 (± 31.89)
Concommitant procedures	36 (83.7%)
CABG	6 (14.0%)
Pacemaker	0 (0.0%)
Other Valve surgery	3 (7.0%)
Tricuspic ring	12 (27.9%)
Maze IV	10 (23.3%)
Left auricle resection	19 (44.2%)
Closure of ASD	4 (9.3%)
Ascending aorta surgery	0 (0.0%)
Other	1 (2.3%)
Alfieri technique	
Central	31 (72.1%)
Anterolateral	2 (4.7%)
Posteriomedial	10 (23.3%)

Categorial data is presented as number of patients (% of the population). Remaining data is presented with a mean value (± SD). ICD = implantable cardioverter defibrillator. ASD = atrial septum defect. Descriptive data can be seen in appendix 7.2.

Table 3 shows the postoperative data with postoperative complications. The patients had a mean in-hospital stay of 10.23 (± 5.25) days. A total of 38 (90.5%) patients had a postoperative NYHA classification of NYHA I or II. Readmission within 30 days was seen in 6 (14.0%) patients and of these three (7.0%) patients were readmitted due to atrial fibrillation, one (2.3%) patient due to pericardial effusion, one (2.3%) patient due to pleural effusion and one (2.3%) patient due to non-specific fever. Freedom of reoperation was seen in 41 (95.3%) patients.

Table 3 – The table shows descriptive postoperative data for 43 patients. Categorial data is presented as number of patients (% of the population). Remaining data is presented with a mean value (± SD). ICD = implantable cardioverter defibrillator. Descriptive data can be seen in appendix X.

In-hospital stay [days]	10.23 (± 5.25)
Post operative complications	23 (53.5%)
Renal insufficiency	2 (4.7%)
Atrial fibrillation	14 (32.6%)

SAM	0 (0.0%)
Myocardial ischemia	0 (0.0%)
Pacemaker	8 (18.6%)
Mitral regurgitation	3 (7.0%)
Stenosis	0 (0.0%)
Stroke	0 (0.0%)
NYHA , N=42	
NYHA I	23 (54.8%)
NYHA II	15 (35.7%)
NYHA III	3 (7.1%)
NYHA IV	1 (2.4%)
Reoperation	
Freedom of reoperation	41 (95.3%)
Reoperation within 30 days	1 (2.3%)
Reoperation within 5 years	1 (2.3%)
Readmission within 30 days	6 (14.0%)
LVEF [%]	
Post operative	51.40 (± 9.90)
3 month follow-up, n=36	51.27 (± 8.64)
Mortality	
Within 30 days	0 (0.0%)
Within 5 years	5 (11.6%)
Cardiac mortality	1 (2.3%)
Non-cardiac mortality	4 (9.3%)

Categorial data is presented as number of patients (% of the population). Remaining data is presented with a mean value (± SD). ICD = implantable cardioverter defibrillator. SAM = systolic anterior motion. Descriptive data can be seen in appendix 7.3.

Postoperative complications were seen in 23 (53.5%) patients, with the most common complication being AF (32.6%) and need of a pacemaker (18.6%) due to arrythmia. The mean postoperative LVEF was 51.27 (±8.64) % after a 3-month follow-up. A paired *t*-test shows a significant (p=0.004) reduction in LVEF post-operative (appendix 7.3.2). Only three patients (7.0%) had postoperative MR and of these, one patient (2.3%) had severe MR and received a valve replacement.

Survival proportion is seen in Figure 2, censoring indicates individual follow-up time.

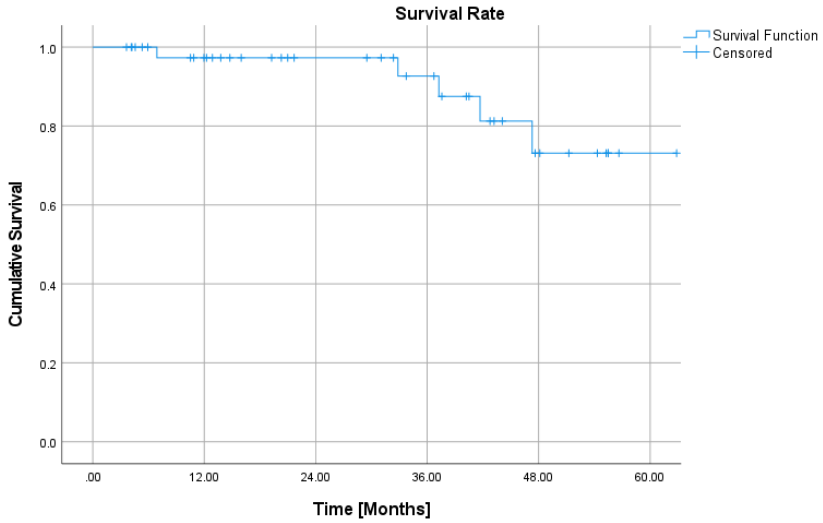

Figure 2 – Figure 2 shows a Kaplan-Meier estimate of survival proportion. Y-axis shows cumulative survival for all 43 patients, while X-axis shows time in months. Crosses marks censoring, which is the time of individual follow-up. Descriptive data can be seen in appendix 7.3.1.

The mean survival time at follow-up at 60 months was 56.04 (± 2.70) months. A total of five patients (11.6%) died. One (2.3%) patient died of cardiac causes, while four patients (9.3%) died of non-cardiac causes. There were no cases of in-hospital mortality.

4 Discussion

In this study, 43 patients received an Alfieri repair for severe MR, with no cases of in-hospital deaths. After a total follow-up time of 60 months there was only one case of cardiac death (2.3%). Four cases of non-cardiac cause mortality (9.3%) were seen, which also affects the survival rate. However, the age and comorbidities of the study population must be considered (table 1). The rate of post-operative complications remained low with no cases of mitral stenosis, stroke, myocardial ischemia, SAM and only two cases of acute renal insufficiency (table 3), which has been reported in other studies (10,13,16,17). The most common post-operative complications were AF and need of a pacemaker (table 3). However, this is a known and prevalent complication to cardiac surgery (5).

Atrial fibrillation is present in about 50 % of patients receiving mitral valve surgery, which is identical with our findings, where 58% were diagnosed with preoperative AF (table 1). AF is associated with a higher NYHA score, a lower LVEF and atrial dilation according to (27). Therefore, concomitant procedures to treat the preoperative AF was frequently used (table 2), since preoperative AF increases mortality in patients undergoing mitral valve surgery due to risk of stroke, thromboembolism and anticoagulant-related haemorrhage. AF can also cause reduced cardiac output and cardiomyopathy (27). Although, with the surgical intervention and elimination of MR, AF as a postoperative complication is more tolerated.

When comparing table 1 and table 3, an improvement in NYHA score is seen. A total of 51.2% (table 1) had a preoperative NYHA score of I or II, while 90.5% (table 3) had a NYHA score of I or II postoperatively. Preoperative LVEF was 57.91 (± 10.87) % with a significant (*p=0.004*) postoperative decrease to 51.40 (± 9.90) %. Although a decrease in LVEF is to be expected postoperatively, as mentioned earlier due to a volumetric adjustment after the elimination of regurgitation jets (5,28) (5). Our results show promising short-term outcome with sustained LVEF, improved NYHA score and reversion of MR for 93.0% (table 3). Only three cases of post-operative MR were seen in this study, with only one of these being severe with the need for reoperation.

Similar results were seen when comparing the results of this study with the postoperative results seen in international studies using the Alfieri repair. De Bonis et. al. (2014) found a significant improvement in postoperative NYHA score, only few cases of residual MR and a low mortality rate (29), similar to the results seen in this study. However, our study had more cases of non-cardiac mortality, while cardiac mortality remained low. The patients from the study by De Bonis et. al. (2014) were younger, had lower preoperative NYHA score and fewer cases of preoperative comorbidities compared to the patient group of this study, which might explain our findings. Although the results are similar, De Bonis et. al. (2014) has a 17-year follow-up, indicating promising long-term results. Similar results were seen in multiple international studies for both short- and long-term follow-ups.(9,11–13,29). Additionally, De Bonis et. al. (2014) tested the effectiveness of the Alfieri repair of the anterior leaflet with good results, however, claiming that a posterior leaflet prolapse repair has shown even better results (29). Only 14.0% in this study received repair for anterior leaflet prolapse, making it statistically difficult to compare to the other groups, without the risk of type I and type II errors.

Associated procedures were performed in 83.7%, which might increase the risk of additional complications, longer CPB, and cross-clamp time. However, a study by Imasaka et. al. (2018) has shown that performing aortic procedures, in addition to an Alfieri repair still shows good results, when comparing to other types of mitral repairs with associated surgery (30). Additionally, concomitant procedures, prolonged CPB, and cross-clamp time, do not seem to affect the quality of the Alfieri repair. The results of this study were comparable to other international studies in regards to residual MR and postoperative mortality (30,31).

A total of 41 (95.3%) received an annuloplasty mitral valve ring and none of these required reoperations. Only two patients did not receive a mitral valve ring because of annular calcification, which was discovered perioperatively. One of these patients had a poor outcome, with readmission within 30 days, severe MR and reoperation after 11 months and three days and no clinical improvement with a pre- and postoperative NYHA score of III.

Multiple studies have found that an Alfieri repair without annuloplasty shows poor results (13,16–18). A Study by Sartipy et. al. (2007), in which, 31 patients did not receive a mitral valve ring (MVR) due to cardiomyopathy. The Alfieri repair had poor results, with a 5-year survival rate of 48 % where most of these were cardiac mortality (16). Similar results were seen in other studies, also with a much higher rate of post-operative complications and residual MR (7,13,16–18). A study by Kuduvalli et. al. (2016) had an in-hospital mortality of 4.8 % and freedom of reoperation of only 80.4 % showing a worse outcome than previously mentioned studies. Only 80.4% of the patients in the study by Kuduvalli et. al. (2016) received an MVR (13). A study by Maisano et. al. (2003) directly evaluated Alfieri repair without a MVR with suboptimal outcomes (7). This confirms that the MVR improves the effectiveness of the surgery, lowers the amount of post-operative complications and stabilises the Alfieri repair long-term (15).

An alternative surgical procedure could be considered, when the outcome is known to be poor due to contraindications. However, other types of repair seem inferior or equal to the Alfieri repair. An Alfieri repair is favourable compared to the loop technique, which repairs the chorda, in patients of higher age and risk of postoperative complications. The Alfieri repair is also significantly faster than the loop technique (32). When comparing the Alfieri repair with valve replacement, a study by Raman et. al. (2003) found that the Alfieri repair was associated with no postoperative complications and no reoperations. The study found a 5-year survival rate of 94.4% with a 90% freedom of reoperations when performing an Alfieri repair compared to valve replacements (14). However, a valve replacement could be preferred in cases of contraindications, as the outcome otherwise is poor.

Changing the surgical approach to a more minimally invasive technique, could be an alternative. In this study only one patient received a thoracotomy while the remaining 42 patients received a midline sternotomy. A sternotomy is a relatively invasive procedure, which increases CPB time, clamp time and in-hospital stay, when compared to other procedures such as transcatheter MitraClip™. Transcatheter MitraClip™ was not used in this study, even though several studies have shown benefits, in regards to mortality, postoperative complications, and time of in-hospital stay (33–35). A study by Malik et. al. (2020) showed a significant difference in in-hospital mortality, fever postoperative complications, and shorter in-hospital stay, when comparing transcatheter MitraClip™ with surgical mitral valve repair (33).

Pighi et. al. (2016) showed short-term results of percutaneous E-to-E valve repair in ischemic and nonischaemic patients. They found that ischemic MR has a worse prognosis with one year mortality of 15.0% and 25.8% rehospitalisation. Therefore, they suggest Transcatheter MitraClip™ for surgical correction (36). Although, a higher rate of residual MR could be expected, this approach is favourable compared to midline sternotomy. Malik et. al. (2020) found a four-times increased mortality rate when using a surgical approach instead of a transcatheter approach in patients above 80 years of age (33), which is relatively close to the mean age of our study population.

Although the transcatheter approach is associated with lower mortality rate, fewer complications and shorter in-hospital stay (33,34), it is also associated with a higher rate of residual MR and higher rate of reoperations in the first year after surgery, when compared to the surgical mitral valve repair (35,37,38). Transcatheter MitraClip™ could also be used to lower the risk of post-operative complications, in patients who cannot receive an MVR or with high Euroscore II. Thereby, accepting a risk of residual MR, but avoiding the poor post-operative outcome.

De Bonis et. al. (2017) showed that surgical access through mini-thoracotomy is as effective as median sternotomy with regard to effectiveness to an Alfieri repair in Barlow's disease, in a relatively young group of patients with low comorbidity (39). Similar results were reported in a study by Torracca et. al. (2005), where a right anterolateral mini-thoracotomy was used as the surgical access. They found a reduced admission time, faster recovery and better cosmetic results according to the patients (40). A less invasive procedure such as the mini-thoracotomy could be considered more beneficial for fragile patients due to a possible reduction in post-operative complications. Therefore, a different surgical approach than the midline sternotomy could be considered for future investigations of possible benefits in MR patients.

4.1 Study strengths and limitations

All source data was collected twice from an existing database and the electronic patient records, by two different individuals, thereby, reducing the risk of typing errors and misinterpretations in data collection. Descriptive data from the database was also cross checked with the surgeon's reiteration of the procedure in the electronic patient journal. This also contributed to a more thorough assessment of the post-operative follow-up and patient information. The Danish electronic patient journal allows assessment of all contacts to the health care system as well as previous an emerged comorbidity before and after surgery regardless of location or institution.

The follow-up of the current study is relatively short with a mean follow-up time of 19.72 (±18.20) months, while other studies have shown follow-ups as long as 21 years (29). The procedure has been conducted since April 25th, 2000 at Aalborg University Hospital, Denmark; however, the hospital administration and the Head of the Department of Cardiothoracic Surgery has only allowed a data collection of the past 5 years due to national legislations. Therefore, long-term results are unknown. Additionally, the study population is hard to compare to other similar studies, as they use a younger

and healthier study population. Although, most international studies using the Alfieri repair have shown both great short-term and long-term results.

Therefore, the collection of data of the past 20 years would allow for long-term results of the Alfieri repair at the Department of Cardiothoracic Surgery, Aalborg University Hospital. This would also increase the size of the study population, as the study only included 43 patients, which would give a more accurate description of the effectiveness of the Alfieri repair. Previous mentioned studies have debated different outcomes based on the location of the leaflet prolapse, however, a larger study population is needed to evaluate and compare the individual outcome for anterior, posterior and central repair.

The size of the study population could also be decided with the cooperation of an international department of cardiothoracic surgery, receiving information about their study population and making a similar enrolment program. This could provide the data needed for a power calculation which could be used for a prospective intervention study for the Alfieri repair. Thereby, directly comparing each department's surgical results to each other and being able to detect a five-percentage difference. This would also reduce the risk of type I and type II errors, caused by a rather small study population.

Not all patients had an available LVEF after 3 months and NYHA score. However, additional information could be collected through telephone or mail questionnaire. Not all patients had a 3-month follow-up after the end of this study. Thereby, not allowing statistical comparison of paired groups. Patients could be asked to participate in a 5-year TEE and clinical follow-up, determining LVEF, NYHA score, comorbidities and other complications. This would allow for a longer follow-up period and better statistical comparison.

5 Conclusion

The results of this study confirm previous international research showing promising short-term results after an Alfieri repair. Although a slight difference in study populations, the results from the danish Department of Cardiothoracic surgery, Aalborg University Hospital, is similar to international results of the Alfieri repair. Postoperative LVEF is still within normal function, NYHA score is drastically improved, rate of readmission and re-operation is low. MR is no longer present for 93.0% (table 3), overall, showing promising short-term results. Similar results were found for all patients, despite the fact that three different surgeons were performing the procedures. This shows that the Department of Cardiothoracic Surgery at Aalborg University Hospital, Denmark, can produce the same results as international studies, regardless of the surgeon. However, a longer follow-up period, larger study population and 5-year post-operative clinical follow-up, is to be desired for more precise and long-term results.

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