

Bentall procedure as a lifesaving surgery: A single center experience

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Received September 19, 2022; Accepted January 9, 2023

DOI: 10.3892/mi.2023.68

Abstract. The Bentall procedure is a surgical technique used in the management of aortic root abnormalities with ascending aorta and aortic valve issues. The present study aimed to evaluate the outcomes of 18 patients treated with the Bentall procedure in a single center. The present study was a single-center retrospective case series conducted over a period of 3 years. The patients had either acute ascending dissection and/or dilated ascending aorta with aortic valve dysfunction. The Bentall procedure was performed via standard median sternotomy. St. Jude Medical composite grafts with a valve were applied in all cases. A total number of 18 patients with either acute ascending dissection and/or dilated ascending aorta with aortic valve dysfunction were included in the study. The age of the participants ranged from 27-60 years. The ratio of males to females was 16:2 (males, 88.8%). The symptoms developed 3-4 days prior to hospital admission. Chest pain was the most common presenting symptom (n=10, 55.5%). Hypertension was the most common risk factor (n=12, 66.6%). In total, 14 cases underwent emergency surgery (77.7%). The emergency surgery was performed in 9 patients within 24 h of arrival owing to the association of aortic root dissection with tamponade. For the other cases, the surgery was performed within 2 and 7 days (n=5, 27.7% and n=4, 22.2%) respectively. Early post-operative complications occurred in 5 patients (27.7%). On the whole, as demonstrated herein, the modifications of the Bentall procedure have a notable impact on decreasing the overall mortality rates. Raising the awareness of clinicians and the

general population as regards aortic dissection may aid in the early referral of patients to specialized centers and may thus decrease the overall mortality rate.

Introduction

The Bentall procedure is a surgical technique used in the management of aortic root abnormalities with ascending aorta and aortic valve dysfunctions. It was first described by Bentall and De Bono (1) in 1968 and subsequently also described by others (2). The technique was typically invented to treat patients with aortic root aneurysms. It was then modified in several aspects. Bentall procedures mainly involve the insertion of a mechanical valve conduit to replace the aortic root. It is regarded as a long-term solution, while it requires long-life anticoagulation (3,4). Aortic root dilatation with or without aortic valve dysfunction may cause spontaneous dissection and rupture of the aorta. The patient is placed in a critical situation with the need for rapid lifesaving intervention. The application of the Bentall procedure with its various techniques provides a positive impact on the result; overall life expectancy has also markedly increased over the past 30 years (5). All the previous repairing modalities, such as plication, supracoronary aortic replacement and aneurysm banding were insufficient to complete the removal of the diseased aortic tissue. These methods resulted in increased post-operative complications and mortality rates (6). In recent years, the Bentall procedure has become the gold standard modality in the management of aortic root replacement. It is one of the most curative surgical procedures in the field of cardiac surgery (7-9). The present study aimed to evaluate the outcomes of the Bentall procedure conducted in a single center among a total of 18 patients.

Patients and methods

Study design. The present study was a single-center retrospective case series. A total of 18 patients with either acute ascending dissection and/or dilated ascending aorta with aortic valve dysfunction were included in the study. Patients were

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Key words: aortic root dissection, aortic root dilatation, chest pain, bicuspid aortic valve

enrolled at the Ibn Al-Bitar Specialized Center for Cardiac Surgery (Baghdad, Iraq) from December, 2017 to January, 2020. Ethical approval was provided by the Iraqi Board of Medical Specialization with the approval no. 00245/2017. Written consent was taken from all included patients to participate in the study.

Patient preparation and analyses. The patients were all initially examined by a general practitioner and then referred to a cardiologist. The cardiologist examined the patients and performed examinations for vital signs, as well as an echocardiography. The results of the echocardiography revealed a bicuspid aortic valve in 14 cases (77.7%). Pericardial effusion ranged from mild to tamponade in 12 patients (66%) and all of the patients had aortic root dissection with severe aortic incompetence. Due to the need for a coronary artery bypass graft, all the cases were discussed in a multidisciplinary team (MDT) meeting with the involvement of cardiac surgeons. The outcome of the MDT meeting was to refer the cases to the cardiac surgeons for proper management. The cardiac surgeons re-examined the patients' results, and any investigation which had been conducted >6 weeks prior was conducted again.

Inclusion criteria. The present study included all the patients with either acute ascending dissection and/or dilated ascending aorta with aortic valve dysfunction that had undergone the Bentall procedure at the center between December, 2017 to January, 2020.

Data collection and analysis. An electronic registry database was used to register the patients' medical records, including demographics, medical summary, investigations, surgical indications, procedure specifications, comorbidities and follow-up information. The data were encoded and descriptively analyzed using the Statistical Package for the Social Sciences (SPSS) version 25.

Surgical technique. The procedures were performed via standard median sternotomy. A cardiopulmonary bypass was conducted by cannulating the ascending aorta and combined with the femoral artery or axillary artery in a direct method, and venous return via right atrium venous cannulation. Axillary cannulation was performed for all cases of aortic dissection and sometimes for certain cases of aneurysms involving the aortic arch. Otherwise, regular ascending aortic cannulation was used. Myocardial protection was provided by simultaneous antegrade and retrograde perfusion using del Nido blood cardioplegic solution, either with crystalloid or mixed with blood (Nephron Pharmaceutical Corporation).

Deep hypothermic circulatory arrest (20 c) was used in all cases that had an aortic dissection. Longitudinal aortotomy was performed just above the sino tubular junction to inspect the ascending aorta, aortic root, aortic valve, intimal tear and the site of dissection. Both the coronary ostia were mobilized and excised with the aortic wall patch to facilitate the re-implantation of the composite graft, aortic cusp resection, the resection of the diseased part of the ascending aorta, and the inspection of the aortic arch condition and aortic valve sizing.

Table I. Baseline characteristics of the patients.

Variable	Mean/frequency
Mean age, years (min-max)	40 (27-60)
Mean body mass index, kg/m ² (min-max)	33 (27-35)
Sex, n (%)	
Male	16 (88.9)
Female	2 (11.1)
Symptoms upon arrival, n (%)	
Severe chest pain	10 (56)
Severe hypotension	6 (33)
Unretrieved	2 (11)
Risk factor, n (%)	
Hypertension	12 (66.6)
Smoking	8 (44.4)
Hyperlipidemia	7 (38.8)
Coronary artery disease	3 (16.6)
Elevated renal indices	8 (44.4)
Chronic obstructive pulmonary disease	2 (11.1)
Diabetes mellitus	6 (33.3)
Atrial septal defect	1 (5.5)
Etiology, n (%)	
Atherosclerosis	2 (11.1)
Aortic root dissection	14 (77.7)
Aortic root dilatation	4 (22.2)
Bicuspid aortic valve	14 (77.7)
Time of surgery, n (%)	
Emergency (within 24-48 h)	14 (77.7)
Elective (1-7 days)	4 (22.2)

The St. Jude Medical composite graft with Valsalva (St. Jude Medical, Inc.) was applied in all the cases. Polyester sutures (2/0) with pledgets in an interrupted manner were used for the implantation of the composite on the aortic root. The coronary ostia anastomosis was performed using a 6/0 prolene suture in a continuous manner. Distal anastomosis of the graft to the aortic arch was performed following fixation of the dissection extension with a 4/0 prolene suture with a pledget in an interrupted manner. The graft anastomosis with a 4/0 prolene suture was conducted in a continuous manner to the aortic arch. Biological glue was used to secure the anastomosis sites and decrease the risk of bleeding.

Results

The age of the participants ranged from 27-60 years, with a mean age of 40 years. The ratio of males to females was 16:2 (males, 88.8%) (Table I). Chest pain was the most common presenting symptom (n=10, 55.5%); of the 10 patients with chest pain, 9 patients had an aortic dissection, and 1 patient had aortic root dilatation and coronary artery disease. The symptoms developed 3-4 days prior to hospital admission. Hypertension was the most common risk factor (n=12, 66.6%). In total, 14 cases (77.7%) had bicuspid aortic valve. Elevated renal indices were

Table II. Data of surgery and outcomes.

Variable	Mean/ frequency
Cannulation process	
Axillary Cannulation	16 (88.9%)
Femoral Cannulation	2 (11.1%)
Procedure	
Median sternotomy, n (%)	18 (100)
Ascending aortic diameter, mm (mean)	48
Cardiopulmonary bypass time, min (mean)	310
Aortic cross-clamp time, min (mean)	220
Extent of resection, n (%)	
Hemi arch	4 (22.2)
Ascending only	14 (77.8)
Concomitant surgery, n (%)	
Coronary artery bypass graft (CABG)	2 (11.1)
Atrial septal defect (ASD) closure	1 (5.55)
Early post-operation complication, n (%)	5 (27.7)
Bleeding and re-exploration	1 (5.55)
Stroke	1 (5.55)
Atrial fibrillation	2 (11.1)
Acute kidney injury	(5.55)
Early mortality (within 30 days)	1 (5.55)

noted in 8 patients (44.4%), with which cardiogenic shock was the cause of six of these. Concomitant heart disease was found in 3 patients (16.6%). A total of 14 cases underwent emergency surgery (77.7%). The emergency surgery was performed in 9 patients within 24 h of arrival owing to the association of aortic root dissection with tamponade. For the other cases, the surgery was performed within 2 and 7 days (n=5, 27.7% and n=4, 22.2%) respectively. The aneurysmal size and extension of aortic dissection were the main indications for axillary cannulation (16 patients, 88.9%) and the femoral site was used for cannulation in 2 patients (11.1%) (Table II).

Early post-operative complications occurred in 5 patients (27.7%). Surgical bleeding and re-exploration occurred in 1 patient (5.55%). Stroke (n=1, 5.55%), atrial fibrillation (n=2, 11.1%) and acute kidney injury (n=1, 5.55%) were also recorded (Table II). The patient with acute kidney injury was managed according to the KIDIGO protocol (10) with continuous renal replacement therapy (CCRT). This was the only patient that passed away during the study. All the variables including, the patients' age, gender, risk factors, etiology, operation data and post-operative data are all summarized in Tables I and II.

Discussion

It is almost six decades since Bentall and De Bono (1) described a novel surgical technique for the management of aortic root aneurysm. After a number of years, the technique, with several additional alternations, had become the gold standard approach in managing abnormalities of the aortic valve, ascending aorta and the aortic root. For that reason,

investigations of the outcomes of the new approaches to the Bentall procedures have been widely suggested (7). The present case series is a single center experience that includes the patients who had an abnormality of ascending dissection and/or dilated ascending aorta. The results were compared to those of previous related studies.

In a case series conducted by Spittell *et al* (11), the majority of the patients had been affected by the aortic dissection during their 60-70 years of life. Males were predominant over females at a 2:1 ratio. Systemic hypertension is regarded as the most common risk factor for aortic dissection. Congenitally malformed aortic valve also plays a significant role in the presentation of aortic dissection. In the study by Spittell *et al* (11), a bicuspid aortic valve was reported in 17 patients. One of the rare causes of congestive heart failure related to aortic dissection is the rupturing of the dissection and extending into the atria or right ventricle. Therefore, patients with acute congestive heart failure that have a history of chest pain should be examined for aortic dissection (11).

Some studies have mentioned the congenital bicuspid valves as a distinctive risk of early aneurysm formation. In the study by Hagl *et al* (7) bicuspid aortic valve was associated with aneurysm formation in almost 50% of the cases. Several other factors, such as arteriosclerosis, diabetes and Marfan syndrome have been reported to be combined with the aneurysm and dissection of the aorta (7,12). The present study differed from the study of Spittell *et al* (11) regarding the age of the patients. Hypertension was the most common risk factor (66.6%) as stated in the previous study. A bicuspid aortic valve was found in 77.7% of the cases. Approximately 78% of the patients had an aortic dissection in that study, but none of the cases were associated with a dissection rupture extending into the atria and the right ventricle.

The instant onset of chest pain is the typical symptom of aortic dissection. It has been reported to present in >94% of patients (13). Some other studies have described lower extremity ischemia as the frequent manifestation of aortic dissection (11,14-16). Chest pain is a universal symptom that can be easily confused with other common illnesses. Aortic root dissection is an uncommon disorder and ranges from 2.6 to 3.5 per 100,000 individuals/year (17,18). These findings can cause patient referral delays and the condition of patients may deteriorate before arrival. Other studies have reported that the mortality rate increases 1-2% for every hour without any treatment (19). Caution should be practiced regarding the pattern of chest pain in a patient with acute aortic dissection. All the cases in our experience had been referred late (2-3 days following the onset of symptoms). Chest pain was the most presenting symptom (55.5%) and 90% of patients had aortic root dissection. This is comparable with the finding of other studies (11,20). The present study reported acute kidney injury in 1 patient (5.5%) who was managed with CRRT. In addition, Etz *et al* (4) reported renal issues required dialysis in 8 patients (2.2%).

There is a low mortality rate associated with the Bentall procedure. The early mortality rate in the study by Gelsomino *et al* (21) was only 5.5% and Benke *et al* (22) reported a mortality rate of 3.4%. Yakut (23) performed aortic root replacement in 80 patients using a flanged composite graft. He reported a mortality rate of 8.75%; the major point to be mentioned is that none of the cases succumbed due to

flange-related complications (23). Some independent risk factors have been reported to be associated with mortality after the Bentall procedure, including hypertension, diabetes mellitus, elderly, severe ventricular dysfunction, Marfan syndrome, dissection, endocarditis, previous cardiac surgery, coronary artery disease and left ventricle ejection fraction (24). Despite the association of several mentioned risk factors with some of the cases in the present study, the mortality rate due to these risks was insignificant. In the present case series, the early mortality rate was (5.5%) due to acute kidney injury complications. The present study reported this percentage of mortality as all the cases were operated on as emergency cases. From the beginning of the practice in the present study, the aortic dissection team was established to take rapid action for emergency intervention. This helped to decrease the preparation time and the mortality rate.

Using composite grafts to replace the ascending aorta may be a low-risk and successful operation when the platelet preservation technique is applied. Previous studies have used coronary artery bypass surgery with aprotinin to decrease the rate of blood losses during both the intra-operative and post-operative period (25,26). In the present study, axillary arterial cannulation was used for all cases with aortic dissection for easy initiation of antegrade cerebral perfusion during circulatory arrest and to reduce the rate of cerebral embolization compared with femoral cannulation. To decrease myocardial oxygen demand and work in a bloodless field to improve myocardial protection during surgery, del Nido blood cardioplegic solution was perfused in an antegrade and retrograde, and the venting of the right upper pulmonary vein and hypothermic circulatory arrest (20c) were used.

In the present case series, post-operative bleeding occurred in 1 patient (5.5%) and this required re-exploration. A stroke occurred in 1 patient (5.5%) and was managed medically. However, Zehr *et al* (27) reported that 8 cases (4%) developed bleeding that required re-exploration. In addition, Etz *et al* (4) reported reopening surgery in 18.3% of the cases due to bleeding. In the present study, cardiac arrest occurred during anesthesia induction for all the cases with tamponade. They were managed with rapid exploration by opening the lower part of the sternum to evacuate the collected blood in the pericardium to relieve the heart compression. No re-exploration due to failure of the Bentall procedure was performed in the present study. Bio glues as fibrin sealant material were used to secure all sutures to decrease the risk of post-operative bleeding; this was also reported in the study by Della Corte *et al* (28).

There have been concerns regarding the risks of hemorrhage owing to the traction on the aortic wall in the classic Bentall procedure (22). Hagl *et al* (7) reported no technical failures in their study and they proposed the Bentall procedure, as a safe and durable technique with a low rate of post-operative complications. Some of the patients in the study by Hagl *et al* (7) required ensuing operations for aneurysms located in different sites of the aorta.

A diligent post-operative follow-up is strongly recommended for patients with disease of the ascending aorta (7). In the present case series, the results were satisfactory following the Bentall procedure. The results of the present study were in accordance with those of the study by Yakut (23). None of the patients succumbed due to the Bentall procedure.

The major limitations of the present study include the small, single-group sample size, the lack of proper data and statistical analysis (quantitative) and variables, the short-term duration of the study, and short or missing post-operative follow-up data.

In conclusion, in accordance with previous studies (21-23), the authors' experience confirmed that the Bentall procedure is a life-saving surgery and it may even be associated with no incident of mortality. Herein, 18 patients with aortic root dissection and dilatation were treated with this procedure. Raising the awareness of clinicians and the general population as regards aortic dissection may aid in the early referral of patients to specialized centers and may thus decrease the overall mortality rate.

Acknowledgements

Not applicable.

Funding

No funding was received.

Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Authors' contributions

AA, SSAM, RO, AM, FHK and OFA were the cardiothoracic surgeons who managed the cases, performed the follow-up of the patients and obtained patient data. FHK, RKA and AMS were involved in the conception of the study, in performing the literature review, and also in the writing of the manuscript. DHMS, BAA, SHM and AM performed the literature review, qualitative data analysis, and examining patient data. All authors have read and approved the final manuscript. OFA and AA confirm the authenticity of all the raw data.

Ethics approval and consent to participate

The present study was approved by the Iraqi Board of Medical Specialization. Written informed consent was obtained from all the patients.

Patient consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

References

1. Bentall H and De Bono A: A technique for complete replacement of the ascending aorta. *Thorax* 23: 338-339, 1968.
2. Kouchoukos NT, Wareing TH, Murphy SF and Perrillo JB: Six-teen-year experience with aortic root replacement. Results of 172 operations. *Ann Thorac Surg* 214: 308-318; discussion 318-20, 1991.

3. Mookhoek A, Korteland NM, Arabkhani B, Di Centa I, Lansac E, Bekkers JA, Bogers AJ and Takkenberg JJ: Bentall procedure: A systematic review and meta-analysis. *Ann Thorac Surg* 101: 1684-1689, 2016.
4. Etz CD, Bischoff MS, Bodian C, Roder F, Brenner R, Griep RB and Di Luozzo G: The Bentall procedure: Is it the gold standard? A series of 597 consecutive cases. *J Thorac Cardiovasc Surg* 140 (Suppl 6): S64-S70; discussion S86-91, 2010.
5. Borulu F and Erkut B: Surgical outcome of patients with ascending aortic aneurysms. *CorSalud* 11: 104-112, 2019.
6. Mldulla PS, Ergin A, Galla J, Lansman SL, Sadeghi AM, Levy M and Griep RB: Three faces of the Bentall procedure. *J Card Surg* 9: 466-481, 1994.
7. Hagl C, Strauch JT, Spielvogel D, Galla JD, Lansman SL, Squitieri R, Bodian CA and Griep RB: Is the Bentall procedure for ascending aorta or aortic valve replacement the best approach for long-term event-free survival?. *Ann Thorac Surg* 76: 698-703, 2003.
8. Cabrol C, Pavie A, Mesnildrey P, Gandjbakhch I, Laughlin L, Bors V and Corcos T: Longterm results with total replacement of the ascending aorta and reimplantation of the coronary arteries. *J Thorac Cardiovasc Surg* 91: 17-25, 1986.
9. Loisançe D: Simplification of the Bentall procedure with surgical and biological innovations. *Eur J Cardiothorac Surg* 8: 613-615, 1994.
10. Khwaja A: KDIGO clinical practice guidelines for acute kidney injury. *Nephron Clin Pract* 120: c179-c184, 2012.
11. Spittell PC, Spittell JA Jr, Joyce JW, Tajik AJ, Edwards WD, Schaff HV and Stanson AW: Clinical features and differential diagnosis of aortic dissection: Experience with 236 cases (1980 through 1990). *Mayo Clin Proc* 68: 642-651, 1993.
12. Yotsumoto G, Moriyama Y, Toyohira H, Shimokawa S, Iguro Y, Watanabe S, Masuda H, Hisatomi K and Taira A: Congenital bicuspid aortic valve: Analysis of 63 surgical cases. *J Heart Valve Dis* 7: 500-503, 1998.
13. Slater EE and DeSanctis RW: The clinical recognition of dissecting aortic aneurysm. *Am J Med* 60: 625-633, 1976.
14. Raby N, Giles J and Walters H: Aortic dissection presenting as acute leg ischaemia. *Clin Radiol* 42: 116-117, 1990.
15. Schneiderman J, Walden R and Adar R: Dissecting aneurysm of the thoracic aorta presenting as iliac artery occlusion. *Vasc Surg* 11: 52-54, 1977.
16. White TJ III, Pinstein ML, Scott RL and Gold RE: Aortic dissection manifested as leg ischemia. *AJR Am J Roentgenol* 135: 353-356, 1980.
17. Kim HJ, Lee HK and Cho B: A case of acute aortic dissection presenting with chest pain relieved by sublingual nitroglycerin. *Korean J Fam Med* 34: 429-433, 2013.
18. Clouse WD, Hallett JW Jr, Schaff HV, Spittell PC, Rowland CM, Ilstrup DM and Melton LJ III: Acute aortic dissection: Population-based incidence compared with degenerative aortic aneurysm rupture. *Mayo Clin Proc* 79: 176-180, 2004.
19. Shirakabe A, Hata N, Yokoyama S, Shinada T, Suzuki Y, Kobayashi N, Kikuchi A, Takano T and Mizuno K: Diagnostic score to differentiate acute aortic dissection in the emergency room. *Circ J* 72: 986-990, 2008.
20. Hagan PG, Nienaber CA, Isselbacher EM, Bruckman D, Karavite DJ, Russman PL, Evangelista A, Fattori R, Suzuki T, Oh JK, *et al*: The International registry of acute aortic dissection (IRAD): New insights into an old disease. *JAMA* 283: 897-903, 2000.
21. Gelsomino S, Morocutti G, Frassani R, Masullo G, Da Col P, Spedicato L and Livi U: Long-term results of Bentall composite aortic root replacement for ascending aortic aneurysms and dissections. *Chest* 124: 984-988, 2003.
22. Benke K, Ágg B, Szabó L, Szilveszter B, Odler B, Pólos M, Cao C, Maurovich-Horvat P, Radovits T, Merkely B and Szabolcs Z: Bentall procedure: Quarter century of clinical experiences of a single surgeon. *J Cardiothorac Surg* 11: 19, 2016.
23. Yakut C: A new modified Bentall procedure: The flanged technique. *Ann Thorac Surg* 71: 2050-2052, 2001.
24. Joo HC, Chang BC, Youn YN, Yoo KJ and Lee S: Clinical experience with the Bentall procedure: 28 years. *Yonsei Med J* 53: 915-923, 2012.
25. Harder MP, Eijnsman L, Roozendaal KJ, van Oeveren W and Wildevuur CR: Aprotinin reduces intraoperative and postoperative blood loss in membrane oxygenator cardiopulmonary bypass. *Ann Thorac Surg* 51: 936-941, 1991.
26. Royston D, Bidstrup BP, Taylor KM and Sapsford RN: Effect of aprotinin on need for blood transfusion after repeat open-heart surgery. *Lancet* 2: 1289-1291, 1987.
27. Zehr KJ, Orszulak TA, Mullany CJ, Matloobi A, Daly RC, Dearani JA, Sundt TM III, Puga FJ, Danielson GK and Schaff HV: Surgery for aneurysms of the aortic root: A 30-year experience. *Circulation* 110: 1364-1371, 2004.
28. Della Corte A, Baldascino F, La Marca F, Scardone M, Nappi G, Cefarelli M, De Santo LS, Pepino P, Cotrufo M and De Feo M: Hemostatic modifications of the Bentall procedure: Imbricated proximal suture and fibrin sealant reduce postoperative morbidity and mortality rates. *Tex Heart Inst J* 39: 206-210, 2012.



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