The Misnomer of Uncomplicated Type B Aortic Dissection

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Abstract

Background: Acute type B aortic dissection (TBAD) is a rare condition that can be divided into complicated (CoTBAD) and uncomplicated (UnCoTBAD) based on certain presenting clinical and radiological features, with UnCoTBAD constituting the majority of TBAD cases. The classification of TBAD directly affects the treatment pathway taken, however, there remains confusion as to exactly what differentiates complicated from uncomplicated TBAD. Aims: The scope of this review is to delineate the literature defining the intervention parameters for UnCoTBAD. Methods: A comprehensive literature search was conducted using multiple electronic databases including PubMed, Scopus, and EMBASE to collate and summarize all research evidence on intervention parameters and protocols for UnCoTBAD. Results: A TBAD without evidence of malperfusion or rupture might be classified as uncomplicated but there remains a subgroup who might exhibit high-risk features. Two clinical features representative of "high risk" are refractory pain and persistent hypertension. First line treatment for CoTBAD is TEVAR, and whilst this has also proven its safety and effectiveness in UnCoTBAD, it is still being managed conservatively. However, TBAD is a dynamic pathology and a significant proportion of UnCoTBADs can progress to become complicated, thus necessitating more complex intervention. While the "high risk" UnCoTBAD do benefit the most from TEVAR, yet, the defining parameters are still debatable as this benefit can be extended to a wider UnCoTBAD population. Conclusion: Uncomplicated TBAD remains a misnomer as it is frequently representative of a complex ongoing disease process requiring very close monitoring in a critical care setting. A clear diagnostic pathway may improve decision making following a diagnosis of UnCoTBAD. Choice of treatment still predominantly depends on when an equilibrium might be reached where the risks of TEVAR outweigh the natural history of the dissection in both the short- and long-term.

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Abstract

Background: Acute type B aortic dissection (TBAD) is a rare condition that can be divided into complicated (CoTBAD) and uncomplicated (UnCoTBAD) based on certain presenting clinical and radiological features, with UnCoTBAD constituting the majority of TBAD cases. The classification of TBAD directly affects the treatment pathway taken, however, there remains confusion as to exactly what differentiates complicated from uncomplicated TBAD.

Aims: The scope of this review is to delineate the literature defining the intervention parameters for UnCoTBAD.

Methods: A comprehensive literature search was conducted using multiple electronic databases including PubMed, Scopus, and EMBASE to collate and summarize all research evidence on intervention parameters and protocols for UnCoTBAD.

Results: A TBAD without evidence of malperfusion or rupture might be classified as uncomplicated but there remains a subgroup who might exhibit high-risk features. Two clinical features representative of "high risk" are refractory pain and persistent hypertension. First line treatment for CoTBAD is TEVAR, and whilst this has also proven its safety and effectiveness in UnCoTBAD, it is still being managed conservatively. However, TBAD is a dynamic pathology and a significant proportion of UnCoTBADs can progress to become complicated, thus necessitating more complex intervention. While the "high risk" UnCoTBAD do benefit the most from TEVAR, yet, the defining parameters are still debatable as this benefit can be extended to a wider UnCoTBAD population.

Conclusion: Uncomplicated TBAD remains a misnomer as it is frequently representative of a complex ongoing disease process requiring very close monitoring in a critical care setting. A clear diagnostic pathway may improve decision making following a diagnosis of UnCoTBAD. Choice of treatment still predominantly depends on when an equilibrium might be reached where the risks of TEVAR outweigh the natural history of the dissection in both the short- and long-term.

Keywords: Type B aortic dissection, TBAD, complicated, uncomplicated, TEVAR

Introduction

Acute type B aortic dissection (TBAD) is a rare disease with minimal data on the incidence in the United Kingdom. However, there is evidence an annual incidence of 550 might be expected for a population of 55 million [1]. It has been subdivided into complicated (CoTBAD) and uncomplicated (UnCoTBAD) depending upon certain presenting clinical features. Interestingly, it is unknown how many TBAD patients initially present as uncomplicated as the disease process may be evolving with clinical and radiological characteristics changing rapidly at times. However, data suggests, up to 75% of TBAD are initially classified as uncomplicated [2]. This is an important issue because once classification has been determined then the optimum treatment plan can be instigated. In the case of CoTBAD, this means that, as well as continuing optimal medical therapy (OMT), an endovascular option should also be considered if the aortic arch anatomy is suitable. However, there remains confusion as to exactly what differentiates complicated from uncomplicated TBAD as very often subtle differences in interpretation of clinical and radiological findings may lead to significant differences in treatment plans. The scope of this review is to delineate the literature defining the intervention parameters for UnCoTBAD.

Uncomplicated type B aortic dissection: Is it a misnomer?

In an attempt to redefine nomenclature associated with TBAD, the Society for Vascular Surgery/Society of Thoracic Surgeons (SVS/STS) produced an up-to-date document in 2020. Complicated and uncomplicated TBAD were defined, as well as high risk features for aortic dissection [3]. An UnCoTBAD was defined as no evidence of rupture or end-organ malperfusion with no associated high-risk features. However, strict definitions for a diagnosis of malperfusion are not wholly established in the literature, and concerns have been raised whether this should be a clinical diagnosis or whether additional imaging is required for diagnosis [4]. Furthermore, radiographic but not clinically apparent malperfusion may be indicative of a poor clinical outcome. Importantly, this "radiographic malperfusion" of the renal or mesenteric beds is a vague finding that may be related to the CT angiography (CTA) phasing and should be interpreted with some caution. It is important to realise a rise in creatinine post TBAD is not necessarily indicative of renal malperfusion.

A TBAD without evidence of malperfusion or rupture might be classified as uncomplicated but there remains a subgroup who might exhibit high-risk features. Two clinical features representative of "high risk" are refractory pain and persistent hypertension. Both are common in the acute presentation of a TBAD and

data from the International Registry of Acute Aortic Dissection (IRAD) indicates almost all TBAD patients present with pain and >70% of that will be located in the chest [5]. Ongoing pain despite adequate opiate analgesia puts a patient in a high-risk category, whilst hypertension despite three different antihypertensives is defined as refractory. Again, in the absence of rupture and malperfusion this situation is classified as a "high risk" aortic dissection.

The "high risk" radiographic findings which have been associated with the risk of developing late aortic complications include >40mm maximal thoracic aortic diameter, a primary entry tear of >10mm, location on the inner curve of the aortic arch and a false lumen (FL) diameter >22mm [6,7]. Furthermore, there are other findings not included in the current criteria for high-risk TBAD, such as the location of entry tear at the concavity of the distal aortic arch in CoTBAD compared to an UnCoTBAD [8,9].

At least 25% of those initially diagnosed as UnCoTBAD may ultimately progress to CoTBAD [10,11]. In addition, there may be a delay of up to 14 days before an initial diagnosis of UnCoTBAD becomes complicated [11]. Despite this, there is evidence that up to 40% of those diagnosed and remaining UnCoTBAD develop aneurysmal dilatation of the thoracic aorta at a mean of 18 months later [12,13]. In this situation, it may be beneficial to develop an early "high risk" change in order that thoracic endovascular aortic repair (TEVAR) is more likely to be performed so that the consequences of late aortic dilatation and rupture might be reduced.

This may have significant consequences as the categorisation of a TBAD to a specific group early on can radically change the treatment plan followed. This might be to the long-term detriment of the patient. One thing which is apparent is that a TBAD is an evolving process and a seemingly straightforward UnCoTBAD can become complicated within a few days. This illustrates the importance of regular observation for clinical change and also a protocol in place for serial imaging to be performed.

The dilemma of TEVAR or OMT in UnCoTBAD

The aim of TEVAR is to seal off the proximal entry tear in the upper thoracic aorta, which is then extended distally, usually to the origin of the coeliac axis. This is done to cover any re-entry tears and to reduce FL pressurisation. However, the risk of spinal cord ischaemia can be an unintended consequence, thus serious consideration must be made to revascularise the left subclavian artery (if covered) and the placement of a spinal drain. Once TBAD has progressed to the chronic stage, TEVAR may no longer be a viable option and either open repair or a branched or fenestrated endovascular option should be considered [14]. What is apparent is that those diagnosed as CoTBAD cannot become an UnCoTBAD because the time until treatment equipoise for TEVAR and OMT or OMT alone for UnCoTBAD is uncertain [15]. The many different radiological and clinical features that emerge early on in the disease process may contribute to this uncertainty.

The optimum treatment for UnCoTBAD is still unknown, especially since the addition of "high risk" features to be considered has led to a more aggressive plan being implemented. It is important to realise the reason for intervention in acute TBAD is to treat the long-term consequences of a pressurised FL. There is evidence that remodelling is most effective in the subacute phase (15-30 days), and if a TBAD is considered for intervention, then it should be performed within the initial 90 days since symptom onset [16,17]. Jubouri et al. [18] recently highlighted the evidence in the literature on the mid- and long-term clinical outcomes of TEVAR in UnCoTBAD, demonstrating its superiority to OMT.

Two prospective randomised trials on UnCoTBAD and TEVAR have been carried out. Both have been criticised for a variety of reasons, including small sample size, lack of long-term follow-up, varying times for stent insertion after the initiating event, and industry led research. The INSTEAD (INvestigation of Stent Grafts in Aortic Dissection) trial randomised 140 chronic UnCoTBAD patients into two groups [19]. The first group was OMT and TEVAR whilst the second group was OMT alone with the primary outcome measure being 2-year mortality rates. Aorta-related deaths, disease progression, and aortic remodelling were all secondary outcomes. Any TEVAR was performed within 2 to 52 weeks with the majority being performed within 10 to 12 weeks. It is worth noting that there was no difference in mortality rates, however, the TEVAR group showed significantly improved aortic remodelling compared to the OMT group (91.3% and 19.4%,

p<0.001). The principal conclusion, however, was that, despite the radiologically improved remodelling, TEVAR provided no considerable advantage over OMT. It should also be noted that the UnCoTBAD patients in this study always reached the subacute stage without any complications developing.

This study was extended to include a 5-year follow up to become the INSTEAD-XL study. Thoracic stent grafting reduced all-cause mortality (11.1% v 19.3%; p=0.13), aorta related mortality (6.9% v 19.3%; p= 0.04) and progression of dissection (27% v 46.1%; p=0.04) relative to OMT alone [20]. Also, complete FL thrombosis was observed in 90.6% of TEVAR group compared to 22% in OMT group. Overall, TEVAR conferred a long-term survival advantage which manifested itself between 2-5 years following the TBAD. Hence, the conclusion was pre-emptive TEVAR in stable patients with an UnCoTBAD should be considered to improve long-term outcomes [20].

The Acute Dissection Stent Grafting or Best Medical Treatment (ADSORB) trial compared OMT to OMT and TEVAR for uncomplicated TBAD [21]. This study specifically examined post intervention aortic morphology with the primary endpoints being FL thrombosis, aortic dilatation and rupture. No deaths occurred in either group within the first 30 days, however, due to disease progression there were three cross overs from the OMT group to TEVAR plus OMT one. After 12 months of surveillance, FL thrombosis did not occur in 97% of OMT patients compared to 57% of the group undergoing TEVAR with OMT. Further evidence showed a maximum FL diameter decrease of 7mm in the TEVAR + OMT group compared to an increase of 4.3mm in the OMT only group. The conclusion was that TEVAR can be safely and effectively used to treat UnCoTBAD [22].

TBAD population risk analysis

The holy grail for the management of UnCoTBAD is to reliably identify those subgroups of patients who are at high risk for aorta-related complications without immediate risk of rupture or malperfusion. Three principal factors have been proposed; an initial aortic diameter of >40mm, an entry tear >10mm and a free-floating TL (this occurs when the entire circumference of the aorta has dissected) [23]. Song et al. [24] showed that the upper descending thoracic aorta is the principal site where aneurysmal dilatation occurs following a TBAD. He also identified a diameter of 22mm of the FL at presentation as a powerful predictor of late aneurysmal change of the thoracic aorta. It was also considered a more accurate predictor for long term complications than the initial overall thoracic aortic diameter. A positive correlation was also identified between the number of proximal entry tears and future thoracic aortic dilatation. A single-entry tear was associated with a higher growth rate of the thoracic aorta [25,26]. This was supported by Ray et al. [27] who published data on UnCoTBAD presenting within 2 weeks of the initial event where the most sensitive indicator for mortality was an aortic diameter >44mm with a FL diameter of >22mm.

Accurate assessment at the time of acute presentation allows TBAD patients to be classified as complicated or uncomplicated. Regular clinical assessments need to be done as well as routine blood tests looking for biochemical markers of hepatic, gut or renal ischaemia. Lower limb weakness may be due to spinal cord vascular compromise or true lumen compression by the FL indicating arterial insufficiency. Due to development of rupture or malperfusion, the UnCoTBAD group may remain uncomplicated or be diagnosed as delayed complicated. Other "high risk" symptoms and signs to evaluate include a primary entry tear >10mm located on the arch concavity, total aortic diameter >40mm and an associated FL diameter of >22mm. Those who have intractable hypertension or ongoing pain following presentation may also benefit from early TEVAR [17,28]. It raises the question on whether these patients should be classified as CoTBAD despite no evidence of rupture or malperfusion. According to the IRAD registry, there is evidence that the presence of hypertension or refractory pain in a UnCoTBAD is associated with an increased mortality rate [29].

Conclusion

Uncomplicated TBAD remains a misnomer as it is frequently representative of a complex ongoing disease process requiring very close monitoring in a critical care setting. A clear diagnostic pathway may improve decision making following a diagnosis of UnCoTBAD. In the absence of rupture or malperfusion (both

clinically and on imaging) a diagnosis of UnCoTBAD can be made. This may then proceed in one of two ways depending on the appearance of rupture or malperfusion and whether high risk features appear on subsequent scans (usually a few days apart). If there is no evidence of the aforementioned then the same initial diagnosis remains. Choice of treatment is very much directed by when equipoise might be reached where the risks of TEVAR outweigh the natural history of the dissection in both the short- and long-term.

References

1. Multidisciplinary team-led management of acute Type B aortic dissection in the United Kingdom. Field ML, Kuduvalli M & Oo A. J R Soc Med 2011:104:53-58.

2. Diagnosis and treatment of uncomplicated type B aortic dissection. Cooper M, Hickes C, Ratchford EV, Slameh MJ & Malas M. Vasc Med 2016;21(6):547-552.

3. Society for Vascular Surgery (SVS) and Society of Thoracic Surgeons (STS) reporting standards for type B aortic dissections. Lombardi JV, Hughes GC, Appoo JJ et al. J Vasc Surg 2020;71:723-47.

4. Outcomes of patients with acute type B (DeBakey III) aortic dissection. Afifi RO, Sandhu HK, Leake SS, Boutrous ML, Kumar V, Azizzadeh A et al. Circulation 2015;132:748-754.

5. The International Registry of Acute Aortic Dissection (IRAD) New insights into an old disease. Hagan PG, Nienaber CA, Isselbacher EM et al. JAMA 2020;283:897-903.

6. Predictors of late aortic events after Stanford type B acute aortic dissection. Kudo T, Mikamo A, Kurazumi H, Suzuki R, Morikage & Hamano K. J Thorac Cardiovasc Surg 2014;148:98-104.

7. An algorithmic strategy for the evaluation and management of type B dissections. Dake MD. Endovascular Today 2014;13:42-52.

8. Early outcomes of the conformable stent graft for acute complicated and uncomplicated type B aortic dissection. Zhu t, Si Y, Fang Y, Chen B, Yang J, Yue J, Fu W. J Vasc Surg 2017 Dec;66(6):1644-1652.

9.A new mechanism by which an acute type B aortic dissection is primarily complicated, becomes complicated or remains uncomplicated. Loewe C, Czerny M, Sodeck GH, Ta J, Schoder M, Funovics M, Dumfarth J, Ehrlich M, Grimm M & Lammer J. Ann Thorac Surg 2012;93:1215-22.

10.A multicentre clinical trial of endovascular stent graft repair of acute catastrophies of the descending thoracic aorta. Cambria RP, Crawford RS, Cho JS et al. J Vasc Surg 2009;50:1255-64:e1251-54.

11. The incidence of delayed complications in acute type B aortic dissections is underestimated. Reutersberg B, Trenner M, Haller B, Geisbusch S, Reeps C & Eckstein HH. J Vasc Surg 2018;68:356-63.

12. The natural history of medically managed acute type B aortic dissection. Durham CA, Cambria RP, Wang LJ, Ergul EA, Aranson NJ, Patel VI & Conrad MF. J Vasc Surg 2015;61:1192-9.

13. TEVAR for chronic aortic dissection – is covering the primary entry tear enough?. Kolbel T, Tsilimparis N, Wipper S et al. J Cardiovasc Surg (Torino) 2014;55:519-527.

14. Endovascular management of chronic post-dissection aneurysms. Oikonomou K, Katsargyris A, Ritter W, Sinelli D, Seto Y & Verhoeven EL. Ann Cardiothorac Surg 2014;3:307-313.

15. Time until treatment equipoise. Noorani A, Hippelainen M & Nashef SAM. JAMA Surgery 2014;149(2):109-111.

16. What is the optimal timing for thoracic endovascular aortic repair in uncomplicated Type B aortic dissection? Jubouri M, Bashir M, Tan SZ, et al. J Card Surg.2022;37:993-1001. doi:10.1111/jocs.16190.

17. Singh S, Palanca JA, Austin NJ, et al.Criteria for endovascular intervention in type B aorticdissection.J Card Surg. 2022;37:987-992.doi:10.1111/jocs.16267992|SINGHET AL.

18. Mid-and long-term outcomes of thoracic endovascular aortic repair in acute and subacute uncomplicated type B aortic dissection. Jubouri M, Al-Tawil M, Yip HCA, et al. J Card Surg. 2022;1-12.doi:10.1111/jocs.16349

19. Randomised comparison of strategies for type B aortic dissection: the INvestigation of STEnt Grafts in Aortic Dissection (INSTEAD) trial. Nienaber C, Rousseau H, Eggebrecht H, Fattori R, Rehders T et al. Circulation2009;120(25):2519-2528.

20. Endovascular repair of type B aortic dissection: Long-term results of the randomised INvestigation of STEnt Grafts in Aortic Dissection (INSTEAD) trial. Nienaber C, Kische S, Rousseau H, Eggebrecht H, Rehders T, Kundt G et al. Circulation: Cardiovascular Interventions. 2013;6(4):407-416.

21.ADSORB: A study on the efficacy of endovascular grafting in uncomplicated acute dissection of the descending aorta. Brunkwall J, Lammer J, Verhoeven E et al. Eur J Vasc Endovasc Surg 2012;44:31-36.

22. Endovascular repair of acute uncomplicated aortic type B dissection promotes aortic remodelling: 1 year results of the ADSORB trial. Brunkwall J, Kasprzak P, Verhoeven E, Heijmen R, Taylor P, Alric P et al. Eur J Vasc Endovasc Surg 2014;48(3):285-91.

23.Predictors of late aortic intervention in patients with medically treated type B aortic dissection. Schwartz SI, Durham C, Clouse D, Patel VI, Lancaster RT, Cambria RP & Conrad MF. J Vasc Surg 2018;67:78-84).

24.Long-term predictors of descending aorta aneurysmal change in patients with aortic dissection. Song JM, Kim SD, Kim JH, Kim MJ, Kang DH, Seo JB, Lim TH, Lee JW, Song MG & Song JK. JACC 2007;50:799-804.

25.Number of entry tears is associated with aortic growth in type B aortic dissections, Tolenaar JL, van Keulen JW, Trimarchi S et al. Ann Thorac Surg 2013;96:39-42.

26.Long-term outcome of aortic dissection with patent false lumen: predictive role of entry tear, size and location. Evangelista A, Salas A, Ribera A et al. Circulation 2012;125:3133-41.

27.Predictors of intervention and mortality in patients with uncomplicated acute type B aortic dissection. Ray HM, Durham CA, Ocazionez D, Charlton-Ouw KM, Estrera AL, Miller CM, Safi HJ & Azizzadeh A. J Vasc Surg 2016;64:1560-8.

28.Outcomes of thoracic endovascular aortic repair for acute type B aortic dissection in patients with intractable pain or refractory hypertension. Laquian L, Scali ST, Beaver TM, Kubilis P, Beck AW, Giles K, Huber TS & Feezor RJ. J Endovasc Ther 2018:25(2);220-229.

29. Importance of refractory pain and hypertension in acute type B aortic dissection. Trimarchi S, Eagle KA, Nienaber CA et al. Circulation 2010;122:1283-1289.