Acute aortic dissection

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We summarise advances in the epidemiology, presentation, pathogenesis, diagnosis, and management of acute aortic dissection. Improved understanding of this problem has been assisted not only by establishment of an international registry but also by progress in molecular biology and genetics of connective-tissue diseases. Advances in endovascular products and techniques have provided new treatment options. Open surgical repair remains the main treatment for dissection in the ascending aorta, whereas endovascular treatment is increasingly being used in dissection that is limited to other parts of the aorta.

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Introduction

Aortic dissection is a potentially critical break in the lining of the main arterial outflow from the heart. The emergency nature of this problem does not easily lend itself to study by randomised controlled trials. The establishment of an international registry and improved understanding of molecular biology and genetics of aortic disease have, however, led to substantial advances in the understanding of this disease (panel 1). The aim of this Seminar is to provide a comprehensive review of acute aortic dissection, concentrating on developments since the last Seminar on this topic in *The Lancet*.[1]

Epidemiology

Population-based studies suggest an incidence of acute aortic dissection of about three cases per 100 000 people per year.[2–4] Clouse and colleagues[2] studied presentation of acute aortic dissection during 14 years in Olmsted County, MN, USA. They estimated that the incidence of acute aortic dissection in the County was 3·5 cases per 100 000 people per year between 1980 and 1994.[2] In a community-based study of three small towns in western Hungary (Sümeg, Tapolca, and Keszthely) between 1971 and 1998, Mészáros and colleagues[3] reported that 84 patients had acute aortic dissection, with an incidence of about 2·9 cases per 100 000 people per year.[3]

A population-based study reported the combined incidence of aortic dissection and aneurysm.[4] This study is of interest since it was done in Sweden, where excellent maintenance of databases and registries combined with a high rate of post-mortem examination in unexplained deaths suggests improved ascertainment of cases.[4] Between 1987 and 2002, 4425 cases of aortic dissection were identified within a population of about 8·7 million, which equates to 3·4 per 100 000 people per year. The yearly incidence of aortic dissection and aneurysm combined increased by 50% in men and 30% in women during these 16 years. The reasons for this increase are unknown but might relate to improved identification of cases, with enhanced imaging or increasing age of the population, or both. Overall about 20% of patients died before reaching hospital, 30% during hospital admission, and a further 20% over the next 10 years.[4]

Both circadian and seasonal variations in the frequency of aortic dissection have been recorded.[5,6] Peak frequency has been reported to be between 0800 h and 0900 h and during the winter months.[5] A similar morning peak has been noted in other acute cardiovascular presentation and has been linked to circadian variation in blood pressure.[7]

Pathophysiology

Information about the mechanisms that underlie acute dissection comes from many sources, and we will discuss findings from case series, imaging studies, post-mortem studies, and pathological examinations of surgical biopsy samples, genetic studies, animal models, and in-vitro studies.[8–36] We have focused on investigations reported since 2003 (22 of the 29 studies).

The relation between aortic aneurysm and dissection has caused substantial confusion. Since pre-existing medial degeneration is an important risk factor for acute aortic dissection, patients could have a thoracic aneurysm before dissection. However, in most cases, (more than 80%) acute dissection develops in the absence of a pre-existing aneurysm. After the development of acute dissection, the false lumen might expand later to form an aneurysm as a complication of the dissection. The International Registry of Acute Aortic Dissection (IRAD) has obtained contemporary

Search strategy and selection criteria

We did a comprehensive review of aortic dissection by searching PubMed and the Cochrane library databases for publications with the terms "aorta" or "aortic" and "dissection" over the past 10 years. We also used the terms "acute" and "aortic syndrome" in further searches, but the initial terms mentioned were more useful in identification of relevant articles. Other search terms used included "type a", "type b", "surgery", "stent", and "fenestration". We preferred systematic reviews of prospective studies when available. For epidemiological data, we selected studies that were population based. For clinical presentation, management, and outcome data, we relied on multicentre registry data and large case series. Selection criteria for case series are provided in the tables when relevant. Information about pathogenesis was compiled from animal, in-vitro, and clinical studies. Since the cause of dissection or transection secondary to external trauma is wholly different to that of spontaneous dissection, we excluded traumatic aortic disease from our search.

Panel 1: New developments and controversies in aortic dissection

Pathological changes and classification

- Animal and human genetic studies suggest an important role of dysfunction in transforming growth factor β in the development of dissection
- Recent classification of aortic dissection combines atherosclerotic ulcer, intramural haematoma, and aortic dissection. However, the inter-relation of these conditions is controversial

Improved understanding of the presentation and outcome of dissection (findings from the International Registry of Acute Aortic Dissection)

- About 10% of patients do not present with typical symptoms of ripping chest pain and pulse deficit
- Data have shown the importance of hypertension as a predisposing factor for dissection, with previous history of atherosclerosis less commonly noted
- In-hospital mortality is worst for old patients and those who present in shock for both types of dissection. Outcome is worst for those with branch-vessel occlusion evident by myocardial ischaemia (type A) or visceral ischaemia (both types)

Developments in diagnosis and management

- Human genetic and biomarkers studies, and findings from animal models, suggest the likelihood of identifying some genetic and biomarker risk factors for dissection over the next decade. Use of animal models is improving the understanding of the pathogenesis of aortic disease and expected to identify improved targets for drug development to stabilise the aortic wall
- New endovascular techniques are being increasingly applied to patients with complicated type-B dissection. Whether endovascular management will become first-line treatment for type A or uncomplicated type-B dissection is controversial

data for the characteristics of large numbers of patients who present with acute aortic dissection.[8–11] Table 1 shows comorbidities identified in patients who present with aortic dissection in the ascending aorta (type A) or more distal aorta (type B) in publications from IRAD.[8–11] The most commonly associated factors are a history of hypertension, old age, atherosclerosis, and previous cardiovascular surgery, especially previous repair of aortic aneurysm or dissection. To truly assess whether these features present in patients with aortic dissection are risk factors, we would need large community-based disease and control groups, but no such population studies exist. The risk factors most probably relate to a combination of inherited and acquired weakening of the aortic media and intimal disease.

Marfan's syndrome is an important risk factor for aortic dissection especially in young patients (table 1). Other inherited disorders, including Ehlers-Danlos syndrome type IV, Turner's syndrome, and less well known connective-tissue diseases, have been associated with aortic dissection but were not studied in the IRAD registry. Bicuspid aortic valve was identified in a few patients in IRAD (table 1) and might explain the increased risk of dissection in patients with Turner's syndrome.[12] Aortic vasculitis, such as Takayasu's or giant-cell arteritis, has also been associated with dissection.[13]

Substantial advances have been made in the understanding of Marfan and related syndromes, which has implications for the understanding of aortic dissection in general.[14] Classic Marfan's syndrome is inherited in an autosomal dominant way with variable penetrance and results from mutations in the gene for fibrillin 1. Fibrillin 1 deficiency was traditionally thought to lead to structural weakening of the extracellular matrix at several sites including the aorta. Studies from mice models of Marfan's syndrome, however, suggest that fibrillins have pleiotropic functions in the extracellular matrix, including control of production and destruction of other matrix elements through their ability to interact with vascular smooth-muscle cells and modulate cytokine activity.[15] Thus in some types of fibrillin 1 mutations in mice, the aorta is normal at birth, but gradual loss of fibrillin 1 results in a secondary phenotypical change in the vascular smooth muscles, release of matrix-degrading enzymes, and inflammation.[16] Genetic variation in fibrillin 1 can also improve the availability of the transforming growth factor β (TGFβ) group of cytokines because of its effect on the function of latent TGFβ-binding protein.[17] Mutations in receptors 1 and 2 for TGFβ have been described in other connective-tissue disorders associated with aortic aneurysm and dissection, including a Marfan-like syndrome and Loeys-Dietz syndrome, suggesting that TGFβ has a more general role in weakening of the aorta.[18,19]

Ehlers-Danlos syndrome type IV is a rare autosomal-dominant inherited defect in synthesis of type III procollagen (*COL3A1*).[20] About 40% of patients with Ehlers-Danlos syndrome type IV have dissection and rupture of different arteries by 40 years of age.[20,21] Similar to fibrillin, the defect in type III collagen probably affects the incorporation of other microfibril components within the aortic media, such as type I collagen, and interaction with vascular smooth-muscle cells.[22] The structural change in elastic arteries resulting from a deficiency of type III collagen also leads to increased circumferential stress, which could be important in promoting dissection.[23]

About 1% of the population has a bicuspid rather than a tricuspid aortic valve.[24] The association between bicuspid aortic valve and aortic dilatation and dissection has been linked to an acquired deficiency of aortic fibrillin, apoptosis of vascular smooth-muscle cells, and upregulation of matrix metalloproteinase.[25,26] Echo-cardiography studies of relatives of patients with bicuspid

aortic valves showed a rate of about 30% of valvular or other cardiovascular anomalies, favouring a substantial genetic role in their development.[27] No clear candidate genes have been identified. There also seems to be a genetic basis for aortic dissection that is not associated with a recognised connective-tissue deficiency syndrome.[28,29] Up to 19% of patients who present with a thoracic aneurysm or dissection have a first-degree relative with a similar history.[29] Such familial thoracic aortic aneurysm and dissection seem to result from many genetic abnormalities, and linkage studies have suggested that genes present at various chromosome locations, including 3p24-25, 5q13-14, and 16p12.2-p13.13, have a role.[29–31] One of the genetic mutation sites identified within 3p24-25 is TGFβ receptor 2, which further strengthens the association between TGFβ and aortic dissection.[32]

The findings of histological examination of biopsies of aortic dissection partly depend on the predisposing risk factors.[13] Cystic medial necrosis is a hallmark histological finding, especially in patients with a pre-existing aneurysm. Microscopic features include decreased vascular smooth-muscle cells, mucoid deposition, elastin deficiency, and fragmentation.[13] Elastin fragmentation and loss of vascular smooth-muscle cells are similar to findings seen in abdominal aortic aneurysm, but inflammation is not a central feature, suggesting that the pathological changes are distinct.[13,33] Deficiencies of fibulin 5 have been noted in the aorta of patients with dissection in whom inherited connective-tissue disease has been excluded, suggesting the general importance of deficiency in microfibrillar components in stimulation of the extracellular remodelling.[33]

The increasing use of high-resolution imaging to assess the aorta has led to the identification of a range of intimal and intramural pathological changes that have been related to dissection, including intramural haematoma and atherosclerotic ulcers.[34,35] Histological examination of aortic ulcers shows noticeable intimal atherosclerosis, which is not a constant finding in biopsy samples from aortic dissection.[13,33–35] Further information from natural history studies with serial imaging should provide better insight into the relation of these pathological changes.

The studies outlined suggest that aortic dissection is the end process of an array of different pathological processes, many of which promote weakening of or increased stress on, the aortic wall, or both. The sequence of events might begin with a tear in a damaged intima. Atherosclerotic ulcers could be an evolving stage in the development of such a tear. Alternatively, disruption of a vasa vasorum might result in an intramural haematoma, which later ruptures into the aortic lumen. As recognition emerges that atherosclerotic ulcer, intramural haematoma, and dissection might be related, a report from an international task force on aortic dissection has lent support to a classification that combines these entities (panel 2).[36] Many dissections probably develop without involvement of an intimal ulcer or intramural haematoma. The exact sequence of events associated with the development of aortic dissection is still controversial, including the relation between penetrating atherosclerotic ulcer, intramural haematoma, and classic aortic dissection.[36] Once a dissection path is started, blood can travel for a variable distance in an antegrade or retrograde manner, or both before re-entering the arterial lumen. The extent of dissection is crucial to define the outcome of this process and thus the treatments needed. Accordingly, the staging of dissection has developed as an important means to define initial treatment plans.

Several systems—including the Stanford and De Bakey classifications—have been developed.[36] Unlike the recently developed Svensson classification, the other two

	Type A (n=617)[8]	Type B (n=384)[9]	Aged <40 years (n=68)[11]
Age (years)	61 (14)	65 (13)	30·7 (6·6)
Age >70 years	194 (31%)	159 (42%)	..
Sex (male)	413 (67%)	274 (71%)	52 (76%)
Hypertension	408 (67%)	303 (80%)	23 (34%)
Atherosclerosis	169 (28%)	140 (38%)	1 (1%)
Previous cardiovascular surgery*	100 (16%)	62 (17%)	8 (12%)
Aortic aneurysm	42 (7%)	68 (18%)	13 (19%)
Marfan's syndrome	38 (6%)	11 (3%)	34 (50%)
Iatrogenic related to coronary catheterisation	34 (6%)	9 (2%)	0
Bicuspid aortic valve	14 (4%)	4 (2%)[10]	6 (9%)
Diabetes	24 (4%)	24 (7%)	0
Previous aortic dissection	21 (3%)	33 (9%)	5 (7%)
Pregnancy	1 (<1%)	1 (<1%)[11]	2 (3%)
Cocaine abuse	1 (<1%)	4 (1%)[10]	0

Data are mean (SD) or number (%). Percentages represent total number for whom data were available. *Previous cardiovascular surgery includes coronary artery bypass surgery, aortic-valve replacement, aortic aneurysm or dissection repair, mitral-valve replacement or repair, or other aortic surgery.

***Table 1*: Presenting features of acute aortic dissection as per the International Registry of Acute Aortic Dissection**

***Panel 2*: Classifications of aortic dissection[36]**

Stanford
- Type A: ascending aorta affected
- Type B: ascending aorta not affected

De Bakey
- Type 1: entire aorta affected
- Type 2: ascending aorta affected
- Type 3: descending aorta affected

Svensson
- Class 1: classic dissection with true and false lumen
- Class 2: intramural haematoma or haemorrhage
- Class 3: subtle dissection without haematoma
- Class 4: atherosclerotic penetrating ulcer
- Class 5: iatrogenic or traumatic dissection

systems provide information about the extent of the dissection rather than the underlying pathological process (panel 2). Since the main consideration in the staging of aortic dissection is whether the ascending aorta is affected, the Stanford system is preferred by many general physicians as a simple guide to whether urgent surgical treatment is needed (figure 1). The most appropriate classification system depends on how it is being used (eg, clinical stage or research), which is still controversial.

In an established aortic dissection the principal complications are aortic rupture, cardiac failure (aortic regurgitation, acute myocardial infarction, or tamponade), and end-organ ischaemia (figure 1). The aorta gives rise to many important branches that supply oxygenated blood to the heart (coronary arteries), arms (subclavian arteries), brain (carotid and vertebral arteries), spinal cord (lumbar arteries), viscera (coeliac and mesenteric arteries), kidneys (renal arteries), and legs (iliac arteries). These branch arteries can become poorly perfused as a result of fixed obstructions to their origin, as would happen if the arterial vessel was avulsed and thrombosed during dissection (static malperfusion). Alternatively, if a branch is perfused by the true or false lumen at the site of an established dissection, the supply to that branch will be affected dynamically by changes in the lumen. Thus, high pressure within a false lumen, for example, could compress the true lumen and induce ischaemia of organs fed from it. Collapse of the true lumen can be a particular issue for coronary artery perfusion, which mainly takes place during diastole. Understanding the mechanisms for this process has become increasingly important with the developing array of potential interventional treatments.

In-vitro studies with plastic models, animal aortas, and post-mortem human aortas, combined with imaging and manometric studies in patients, have provided information about the mechanisms underlying malperfusion and factors that affect the outcome of the true and false lumen.[37–39] These studies have shown that the effect of dissection on perfusion to a branch artery is complex, dependent on whether the artery is perfused by

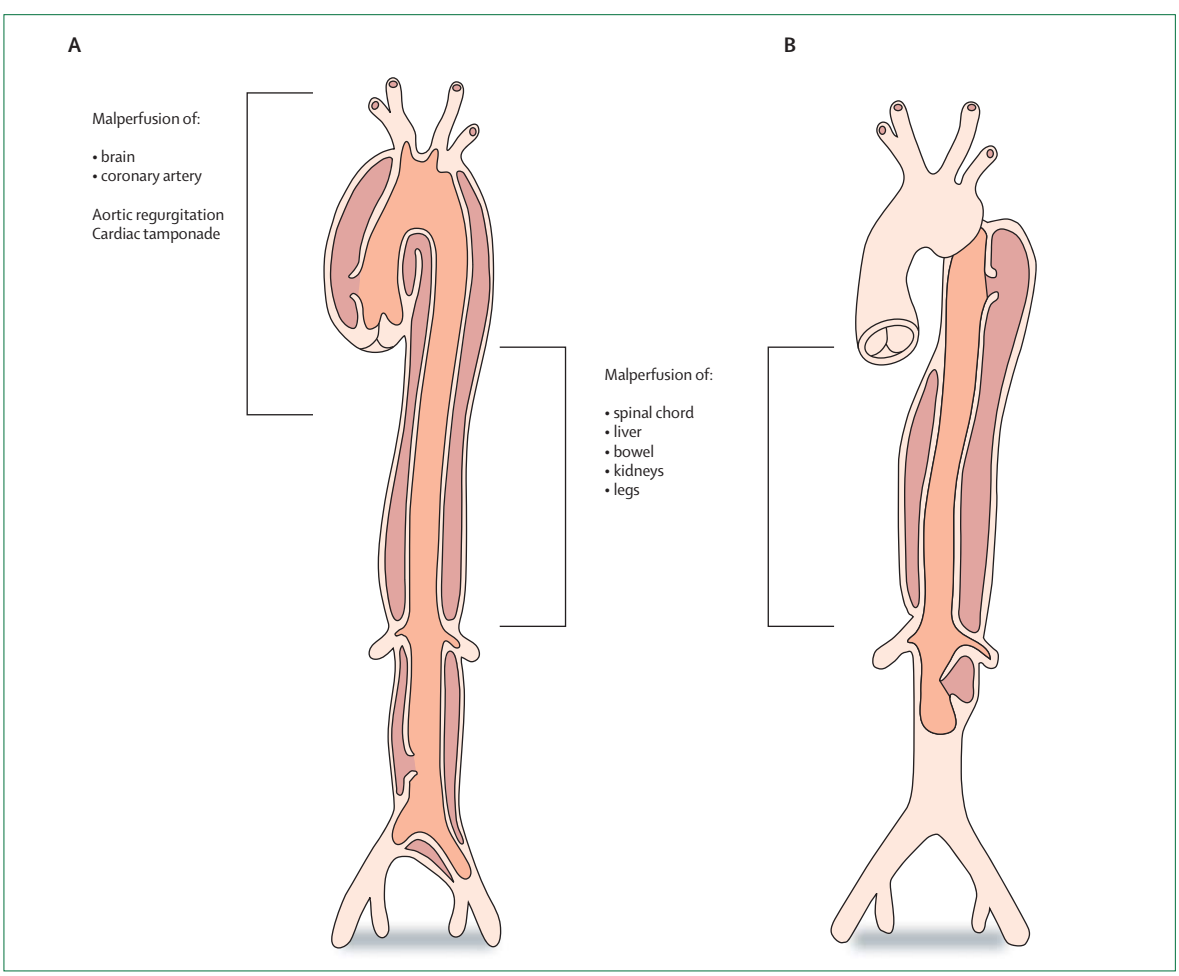

***Figure 1*: Classification and complications of acute aortic dissection**
(A) Type A and (B) type B acute aortic dissection. Type A but not type B dissection affects the ascending aorta.

the false or true lumen, relative collapse of the true lumen, and relation of the intimal flap to the branch artery. Ischaemia of branches being fed by the true lumen is most likely when a dissection affects a wide circumferential extent of the aorta and when there is an increased pressure within the false lumen. This pressure is due to a fairly large entry site compared with a smaller exit site for blood perfusing the false lumen. These findings have helped to promote the notion that expansion of the true lumen is enhanced by reducing inflow to the false lumen.[38]

Static obstruction of aortic branches can take place when dissection is associated with the origin of a branch vessel or extends into the artery, which might result in thrombosis of the vessel. CT and MR angiography can be used to assess whether the branch arteries are being fed by the false or true lumen, and to identify collapse of the true lumen and thrombosis of the branch artery.[40] Imaging findings could thus guide the interventionalist in manoeuvres that are likely to be successful in achieving revascularisation, dependent on the mechanism of ischaemia.

Presentation and diagnosis

Table 2 shows the main presenting symptoms of acute aortic dissection.[8–11,41–43] Although patients usually present with chest pain, which might be described as sharp, tearing, or ripping, the presentation is diverse and about 10% do not complain of pain.[43] Hypotension or shock is seen in about a quarter of patients with acute type A dissection at presentation, whereas hypertension is a more common finding in those who have type B dissection.[43] Other findings from patient history or examination—such as migratory pain, absence of pulses, neurological deficit, aortic regurgitation, cardiac failure, and acute abdominal signs—are less commonly present (table 2). Additional symptoms can relate to underlying connective-tissue disease, such as palate or uvula abnormalities, skin laxity, skeletal abnormalities, and lens dislocation.[14,18] Patients with acute aortic dissection commonly present with chest pain alone, and since about 8% of visits to emergency departments are for this symptom, diagnosis on the basis of history and examination is not straightforward.[44] Early accurate diagnosis is important because urgent surgical intervention might be needed. Thus rapid, cheap, accurate non-invasive tests, which can be done at the bedside, are ideal for initial diagnosis. Various investigations—including blood assays, electrocardiogram (ECG), chest radiography, CT, and echocardiogram—are done in most patients who present with suspected acute aortic dissection.[8,43] Unfortunately, the sensitivity and specificity of ECG and chest radiography is too low to definitively establish or exclude the diagnosis (table 2).

The development of a blood test or biomarker to aid in the diagnosis of aortic dissection is of increasing interest. Promising initial findings have been reported for some novel markers including elastin fragments, D dimers, and smooth-muscle myosin heavy-chain protein.[45–47] For example, smooth-muscle myosin heavy-chain protein was reported to have a sensitivity of 98% and a specificity of 83% for diagnosis of acute aortic dissection.[47] Since aortic dissection is a rare but potentially lethal cause of chest pain, any test needs to be nearly 100% sensitive, ideally also with good specificity.

Large, multicentre prospective studies are underway to explore the diagnostic accuracy of various biomarkers before their role in diagnosis can be defined. How important such biomarkers will become in diagnosis, when they should be measured, and what role they will have in prediction of outcome is unknown. CT angiography or echocardiography is usually needed in patients in whom acute aortic dissection is clinically suspected on the basis of presentation and initial investigations.[8–11,41–43] A systematic review of the diagnostic accuracy of transoesophageal echocardiography, CT angiography, and MRI reported a mean sensitivity and specificity of more than 95% for all three investigations.[48] MRI was slightly better than were the other two at showing aortic dissection in a patient at high pretest probability, whereas CT was better at correctly excluding an aortic dissection in a patient at low pretest probability. In addition to assisting in the diagnosis of aortic dissection, the results of imaging can help to plan management. Important findings include the extent of

	Type A (n=617)[8,41]	Type B (n=384)[9]	Overall (n=1001)
Symptoms and signs			
Chest or back pain	507 (85%)	328 (86%)	835 (85%)
Severe or worst-ever pain	211 (90%)*	135 (90%)*	346 (90%)*
Abrupt onset of pain	453 (91%)	332 (89%)	785 (90%)
Migrating pain	85 (15%)	90 (25%)	175 (19%)
Pain presenting within 6 h of symptoms	334 (79%)	..	..
Any focal neurological deficit	105 (17%)	18 (5%)	123 (12%)
Hypotension, shock, or tamponade†	163 (27%)	13 (3%)	176 (18%)
Hypertension at presentation†	99 (36%)*	260 (69%)	359 (49%)
Any pulse deficit	168 (31%)	73 (21%)	241 (27%)
Aortic regurgitation	117 (44%)	20 (12%)	137 (32%)
Abdominal pain	60 (22%)	73 (43%)	133 (30%)
Chest radiography			
Widened mediastinum	331 (63%)	202 (56%)	533 (60%)
Abnormal aortic contour	124 (47%)*	171 (49%)	295 (48%)
Normal	67 (11%)‡	74 (21%)	141 (16%)‡
Electrocardiography			
Normal	188 (30%)§	113 (31%)	301 (30%)
Left ventricular hypertrophy	139 (23%)§	56 (32%)*	195 (26%)
Myocardial ischaemia or infarction	149 (24%)§	38 (10%)‡	187 (17%)‡

Data are number (%), and are from reference 8, which included 617 patients. Percentages represent total number for whom data were available. *Based on data from reference 43. †Systolic blood pressure ≥150 mm Hg or <100 mm Hg. ‡Based on data from reference 42. §From reference 41, which included 682 patients.

Table 2: **Risk factors of acute aortic dissection from the International Registry of Acute Aortic Dissection registry**

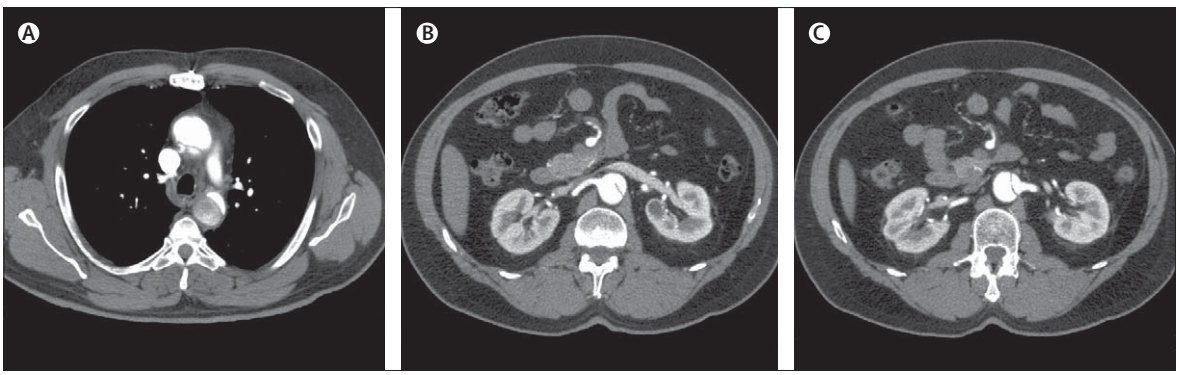

Figure 2: **Computed tomography (CT) findings in aortic dissection**
(A) Axial CT image shows a crescent-like true lumen compressed by an expanded false lumen. (B) Axial CT image shows the right renal artery perfused by the false lumen plus the true lumen via a fenestration in the dissection. (C) Axial CT image shows the left renal artery fed from a collapsed true lumen.

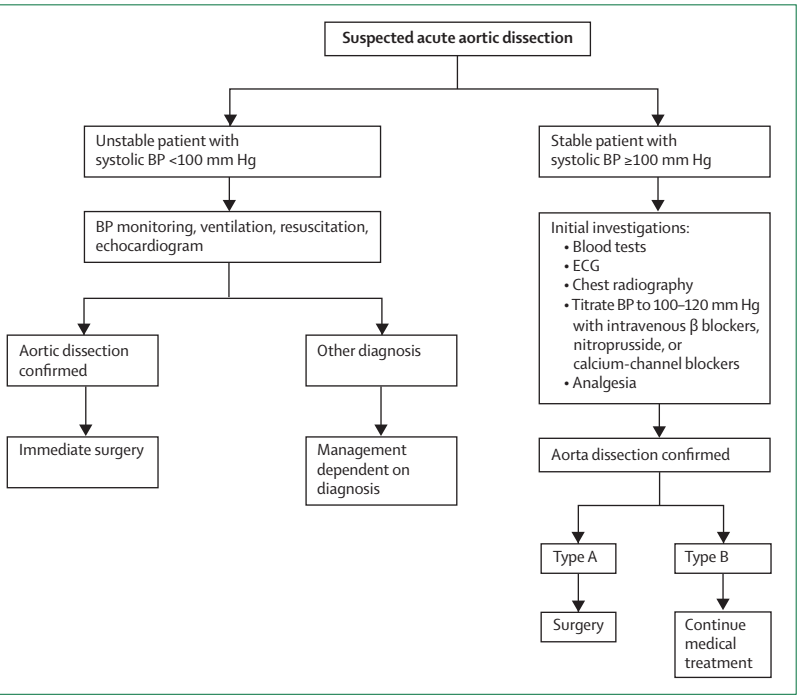

Figure 3: **Initial management pathways in suspected acute aortic dissection**
BP=blood pressure. ECG=electrocardiogram.

the dissection, the size of the true and false lumen, localisation of the intimal tear, the involvement of aortic branches, the presence and extent of aortic regurgitation, and the presence of periaortic haematoma, mediastinal haematoma, or effusion.

The choice of imaging method depends on patients' presentation, local availability of imaging equipment, and staff expertise in interpretation of the imaging. CT angiography can be rapidly done; is available in most hospitals; and provides important information about the extent of dissection, relation between the true and false lumen, and aortic branch compromise (figure 2). Thus, CT angiography is often done in patients in whom a dissection is diagnosed by echocardiography before making any management decision. The introduction of 64-slice multidetector CT with ECG gating has allowed the simultaneous imaging of the aorta and coronary and pulmonary arteries, with the potential to accurately diagnose coronary atherosclerosis, pulmonary embolism, and aortic dissection in one method.[49] Thus, CT will probably remain the first choice for diagnostic testing in most centres.[49] Serial follow-up imaging is important in patients with aortic dissection, and MRI has the advantage of avoiding ionising radiation. Guidelines recommend the use of echocardiography or CT, or both, in the initial imaging of patients suspected to have acute aortic dissection, whereas MRI is favoured for the assessment of chronic dissection.[36] Contrast angiography is recommended in patients in whom visceral malperfusion is suspected or percutaneous interventions are being considered.[36] In practice, angiography might form part of concurrent endovascular therapy.

Management and outcome

No randomised trials have been reported to guide management of aortic dissection. Thus clinical pathways are based on results reported in case series and registries, consensus documents, systematic reviews, and local expertise. In 2001, the European Society of Cardiology published guidelines for the diagnosis and management of aortic dissection that were based on a task force of 11 representatives of appropriate international societies.[36] These guidelines remain the only society-based consensus document for the management of aortic dissection (figure 3 and panel 3), although the American College of Cardiology and American Heart Association Task Force on Practice Guidelines is developing a guideline for management of thoracic aortic diseases.

After initial management and imaging, patients with type B aortic dissection are usually managed medically in an intensive-care unit. Exceptions include patients with signs of aortic rupture, evidence of substantially impaired perfusion of gastrointestinal tract or legs, and uncontrolled hypertension despite medical treatment; percutaneous or open surgical intervention is commonly recommended for these patients.[36] A priority in medical

management is to maintain systolic blood pressure between 100 mm Hg and 120 mm Hg in an attempt to stabilise the dissection and discourage aortic rupture. Close monitoring for signs of aortic rupture or malperfusion, including repeat imaging, is important. β blockers—such as propranolol, metoprolol, labetolol, and esmolol—are usually preferred to control initial blood pressure. In patients with asthma, calcium-channel blockers, such as verapamil or diltiazem, might be preferred. In refractory hypertension, sodium nitroprusside often proves effective, although some physicians believe this complication to be an indication for surgical intervention.

Surgical resection of the ascending aorta is standard management of type A dissection.[36] In case series of patients, only those with several comorbidities and who are moribund or refusing surgery are typically treated medically alone, with reported in-hospital mortality for these patients of about 50% by 30 days.[1] 18% of patients with type A dissection in IRAD, for example, were treated medically, because of comorbidities (33%), patient or family choice (25%), advanced age (21%), or the presence of intramural haematoma alone on imaging (21%).[8,41] Mortality for this group was 58%.[41] The principal aim of surgery for acute type A dissection is to resect the ascending aorta and arch if affected by the intimal tear and to replace it with a prosthetic graft.[36] Repair or replacement of the aortic valve is also needed if substantial pre-existing pathological change of the aortic root or valves exists. Depending on the anatomy and state of the coronary ostia, reconstruction of the coronary arteries is sometimes necessary when aortic-valve replacement is needed. The exact surgical approach will depend on several factors: the preoperative condition of the patient; pre-existing pathological condition predisposing to dissection; extent of the intimal tear and dissection; state of the aortic root, aortic valves, and coronary arteries; and experience and preferences of the surgeon.[36,50] Not surprisingly, many surgical approaches are used in large multicentre series.

IRAD reported the results of surgical repair of acute type A dissection in 682 patients treated at 18 tertiary centres in six countries.[41] Techniques used included right hemiarch replacement (27%), aortic-valve replacement (24%), and coronary arteries' bypass (15%).[41]

One of the controversies in elective surgical repair of ascending aortic aneurysms is whether to repair the aortic valve or to replace it.[50,51] Preservation of the patient's native aortic valve has the major advantage of avoiding the need for long-term anticoagulation, but the frequency of late reoperation can be high.[51] In view of the complex nature of the surgery to resuspend the aortic valve, valve-sparing surgery was done in only 9% of patients with acute dissection in IRAD.[41] Another controversy in surgical management of type A dissection is the extent of distal resection to be done.[52] The dissection frequently extends beyond the ascending aorta and arch, and thus the false lumen might remain patent after ascending aortic replacement.[52] With the substantial mortality and morbidity associated with resection of large parts of the aorta, there is increasing interest in combining open surgical repair of the ascending aorta with endovascular stent grafting.[52–54] These procedures might be combined or staged; however, the exact role of this combined procedure in management is unclear.[52] Overall in-hospital mortality after conventional surgical treatment of type A dissection in a report from IRAD was 24%.[41] Table 3 shows the risk predictors of outcome for patients with type A dissection (overall and those undergoing surgery) compared with those for type B dissection.[9,41,55,56] Patients who were unstable before operation because of shock, tamponade, stroke, or myocardial, renal, or mesenteric ischaemia had a 30% mortality, compared with 15% for stable patients.[41] Similar in-hospital mortalities of 20–30% have been reported in other surgical series, and about 55% of patients return to independent living.[57–60]

Panel 3: Management of acute aortic dissection

- Initial management of suspected acute aortic dissection needs high clinical suspicion and imaging by transoesophageal echocardiography or computed tomography, or both
- Dissection involving the ascending aorta (type A) is usually treated by urgent replacement of this artery along with aortic-valve replacement or repair if needed
- Management of acute aortic dissection that does not involve the ascending aorta (type B) is controversial. Most experts favour medical therapy with strict control of blood pressure and intervention only for complicated patients in whom aortic rupture is suspected or shown. Some physicians favour stent-graft placement to cover the aortic dissection in most cases. Clear evidence of the value of this approach over an initial strategy of medical treatment is lacking

	Type A		Type B	
	Overall	Surgery	Overall	Surgery
Age ≥70 years	1·70 (1·05–2·77)	1·98 (1·19–2·77)	1·56 (0·67–3·61)	4·32 (1·30–14·34)
Past history of AVR	NS	4·21 (1·56–6·34)	NS	NS
Renal failure	4·77 (1·80–12·6)	NS	NS	NS
Presenting with hypotension, shock, or tamponade	2·97 (1·83–4·81)	3·23 (1·95–5·37)	23·80 (10·31–54·94)	6·05 (1·12–32·49)
Migrating chest pain	NS	2·42 (1·32–4·45)	NS	NS
Abrupt onset of chest pain	2·60 (1·22–5·54)	NS	NS	NS
Any pulse deficit	2·03 (1·25–3·29)	1·75 (1·06–2·88)	NS	NS
Myocardial ischaemia or infarction	1·77 (1·06–2·95)	1·76 (1·02–3·03)	NS	NS
Absence of back or chest pain	NS	NS	3·51 (1·30–9·52)	NS
Branch vessel involvement	NS	NS	2·92 (1·21–6·99)	NS

Data are odds ratio (95% CI). AVR=aortic valve replacement. NS=not significant.

Table 3: **Independent predictors of in-hospital mortality at admission in all patients and those selected for surgery with acute type A or B aortic dissection as per International Registry of Acute Aortic Dissection[9,41,55,56]**

	Emergency surgery	Emergency endovascular treatment	In-hospital or 30-day mortality	Mean follow-up (months)	Late operation	Late survival (5 years)*	Death from aortic rupture, dissection, or late repair
1995–2006 (n=180)[63]	7 (4%)	..	13 (7%)	51	31 (17%)	84%	8 (4%)
2001–06 (n=159)[64]	21 (13%)	2 (1%)	14 (9%)	20	11 (7%)	75%	..
1996–2000 (n=384)[9,65]	56 (15%)	46 (12%)	50 (13%)	28	..	80%†	..
1963–99 (n=189)[66]	67 (35%)	37 (20%)	43 (23%)	54	17 (9%)‡	60%	17 (9%)
1988–97 (n=130)[67]	41 (32%)	..	14 (11%)	50	36 (28%)	65%	..
Total (N=1042)	192 (18%)	85 (12%)	134 (13%)	..	95 (14%)	65%	25 (7%)

Data are number (%), unless otherwise specified. All series had cohort sizes of greater than 100 patients, and reported early and late outcomes in the past 5 years. *Reported from Kaplan-Meier analysis. †At 3 years, excludes early deaths. ‡At 5 years.

Table 4: **Outcomes in patients who presented with acute type B dissection in various centres**

Because of the poor outcomes associated with resection of the descending aorta for acute type B dissection and the reasonable overall results for medical treatment, open surgery has been reserved for patients with complications including aortic rupture and malperfusion of mesenteric arteries, renal arteries, or arteries of the legs.[56,61] Resection of the whole aortic area involved in the dissection is usually impossible; thus, patients generally still have perfusion of the false lumen after resection.[62] The European Society of Cardiology's guidelines recommend surgery when aortic rupture is suspected or when shown by the clinical picture or imaging findings of periaortic haematoma or acute aortic expansion.[36]

In a report from IRAD of 476 patients who presented with type B dissection to 18 referral centres, 11% underwent surgery.[56] Indications for surgery (several in a third of patients) included aortic rupture (23%), ischaemia of the viscera (24%) or limbs (16%), extension of the dissection (52%), refractory pain (41%), and uncontrollable hypertension (16%). In-hospital deaths of about 13% have been reported with a general strategy of primary medical therapy, with surgery reserved for patients who develop complications (table 4).[9,63–67] Table 3 shows risk predictors of outcome of surgery.

The success of endovascular treatments in managing disease of the coronary artery, abdominal aorta, and arteries of the legs has encouraged the increasing use of catheter-based therapies in the treatment of aortic dissection.[68–73] Two main approaches have been developed that are complementary to each other. First, covered stents can be directed at the entry site of the dissection. Second, bare-metal stents, balloons, and fenestration techniques can be directed at the branch vessels and false lumen.

One of the guiding principles of open surgical repair of type A dissection is the need to resect the intimal tear, thereby potentially eliminating entry of blood into the false lumen, reversing collapse of the true lumen, and thus eliminating dynamic obstruction of aortic branches and stabilising the dissection.[36–39] After initial experiments in animal and in-vitro models,[38] the use of covered stents originally designed for the treatment of aortic aneurysm was investigated in human patients.[68,69] One or more covered stents are placed over the intimal tear through which blood flows to the false lumen. Additional stents are often used to hold open the true lumen, cover additional entry sites (figure 4), and promote thrombosis of the false lumen. The aim is to direct flow into the true lumen and promote favourable remodelling of the aorta. This approach is being increasingly used in patients with type B dissection.[68–73] Table 5 lists some examples of the results of stent grafts, mainly used in patients with complications of type B dissection,[70,72,73] which are now also being used to treat those without complications.[71] The early results of these techniques are encouraging, with successful exclusion of blood from the false lumen and remodelling of the aorta reported during 12–24 months.[68–73]

The characteristics of grafts placed in the proximal thoracic aorta need to be quite different from those in the abdominal aorta. Improved flexibility and fixation are important for stents placed near the aortic arch. A range of covered stents are under investigation with new devices under development. Two systematic reviews have assessed the results of stent grafts in the management of type B dissection.[74,75] Both reports included patients with acute and chronic dissection in which the indications and results of intervention might be quite different. Reported overall outcomes from both reviews were similar, with 5% in-hospital mortality, 2% stroke, and 1% paraplegia.[74,75] Overall, 11% had major inpatient complications (life-threatening or needing major intervention).[74] The results might be less favourable in patients with acute dissection than in those with chronic dissection (table 5).[74] Many investigators have reported the serious complication of transformation to type A dissection after stent-graft placement for type B dissection, with an estimated rate of 2%.[74] Aorto-oesophageal fistula has also been reported after placement of a stent graft in the thoracic aorta.[76] Long-term reports of follow-up after stent placement have been scarce (table 5). In a systematic review over a mean follow-up of 20 months, 12% of patients needed re-intervention, and aortic rupture occurred in 2%.[74] Survival at 1 year was 90%. These findings emphasise the need for extended follow-up and imaging after endovascular therapy. The fairly favourable in-hospital results have encouraged the use of covered stents for

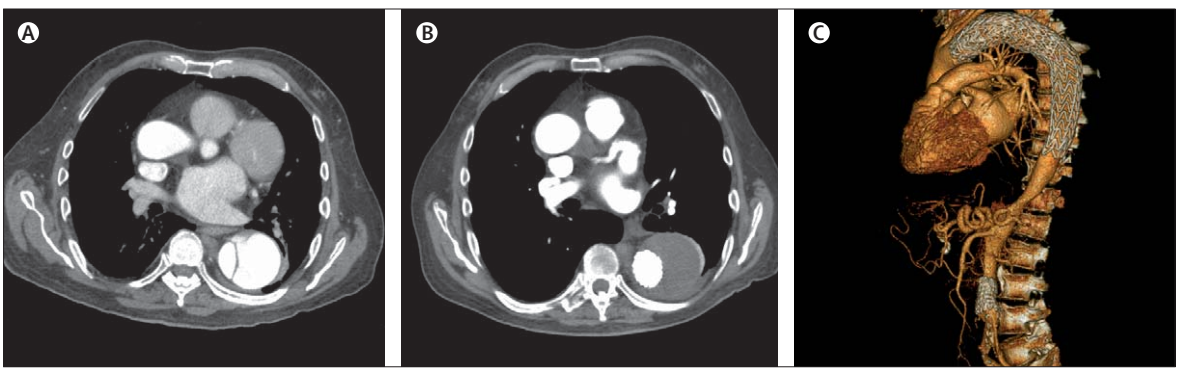

Figure 4: **Computed tomography (CT) findings from a patient after stent-graft repair of aortic dissection**
(A) Axial CT image showing a huge false and collapsed true lumen after aortic dissection. (B) Axial CT image showing a stent graft within the true lumen and a thrombosed false lumen. (C) Three-dimensional reconstruction showing many stent grafts, which were placed in this patient to treat an acute aortic dissection (most proximally but also one distally). A residual stenosis is present within the proximal abdominal aorta.

uncomplicated type B dissection, although this practice remains controversial.

The INvestigation of STEnt grafts in patients with type B Aortic Dissection (INSTEAD) trial was designed to compare covered stents with medical therapy alone for uncomplicated type B dissection.[77] Preliminary results suggested equivalent mortality in patients with uncomplicated acute type B dissection who were treated medically or by endovascular stents and medical therapy at 1 year.[78] Many questions remain about the use of stent-graft combinations in aortic dissection (panel 4).

A range of complementary endovascular techniques have also been described for managing patients with malperfusion secondary to aortic dissection.[82,83] Dynamic obstruction of branch arteries can result from high pressure within the aortic false lumen.[38,39] Both balloon-directed and guidewire-directed scissor techniques have been reported to successfully widen the re-entry site and expand the true lumen resolving dynamic branch stenosis.[82,83] Similarly, bare-metal stents have been used to open branch arteries occluded or narrowed by dynamic or static obstruction in dissection.[83] The indication and value of these procedures is controversial. The techniques, however, add important percutaneous methods with potential to improve outcome in severely ill patients who might have few other options.

Follow-up, treatment, and long-term outcome

Many patients who present with acute aortic dissection are young, with about 60% younger than 70 years (table 1). Aortic rupture of the weakened dilated false lumen, recurrent dissection, and refractory hypertension are the main concerns during long-term follow-up. Clear data for the risk of these problems over the subsequent 10–20 years after initial management are scarce because of the shortage of large prospective series reporting extended follow-up and difficulties with ascertainment of cause of death. Estimates of 10-year survival in studies with mean follow-up of about 5 years varied substantially between 35% and 70%.[63,66] For patients with type A dissection, long-term outcome is less favourable for those with a history of previous cardiac surgery or atherosclerosis.[84] However, for patients with type B dissection, long-term outcome is least favourable for women, those

	Indication			Number of stents	Emergency surgical conversion	In-hospital mortality	Complete false lumen thrombosis	Mean follow-up (months)	Late re-operation	Survival at 1 year	Late aortic rupture or dissection
	Rupture or prominent aortic dilatation	Malperfusion	Other*								
Sweden[70]† (n=67)	32 (48%)	20 (30%)	15 (22%)	6	..	12 (18%)	21 (49%)‡	14	5	..	0
Beijing[71] (n=63)	4 (6%)	0	59 (54%)§	5	0	2 (3%)	62 (98%)	12	0¶	89%	1
Nanjing[72] (n=62)	15 (24%)	..	..	2	0	3 (5%)	..	27	..	94%‖	0
EUROSTAR and UK registry[73] (n=60)	57 (95%)**	17 (28%)**	1 (2%)‖	..	..	7 (12%)	56 (93%)	12	1	90%††	..
Total (N=252)	108 (43%)	37 (19%)	75 (39%)	..	0	24 (10%)	139 (73%)	16	6 (3%)	91%	1 (<1%)

Data are number (%), unless otherwise specified. Series selection was based on cohort size greater than 50, results assessable for patients with acute type B dissection (most reports included a combination of pathologies including chronic dissection and aneurysm), and reported in the past 5 years. *Unless stated includes persistent or recurrent pain, uncontrollable hypertension, and intramural haematoma. †Multicentre. ‡These data were not obtained for all patients. §These patients were selected on the basis of anatomical criteria alone, and were not reported to have a recognised complication of dissection. ¶Four patients needed a second stent 1 week after the initial procedure. ‖At 2 years. **Many indications. ††Excludes inpatient deaths.

Table 5: **Outcomes of stent-graft treatment of acute type B dissection in various centres**

***Panel 4*: Questions about stent-graft combinations**

- What is the most appropriate graft type?
- Should a covered stent simply be placed at the entry site to the false lumen, or are additional bare-metal stents needed along the whole length of the dissection?[79]
- Does the re-entry site need to be covered?
- Are stent grafts appropriate in uncomplicated type B dissection?
- Will covered stents have an important place in the management of type A dissection either as primary treatment or in combination with open surgery?[80,81]

with pre-existing aortic aneurysm or atherosclerosis, and those who develop renal failure or shock while they are in hospital.[65] Partial thrombosis of the false lumen has also been related to poor outcome for type B dissection but not for involvement of the aortic arch.[85,86]

On the basis of the data from patients with Marfan's syndrome, long-term β blockade is usually recommended in patients with aortic dissection to maintain blood pressure less than 130/80 mm Hg.[87] Clinical trials investigating angiotensin II blockers are underway because of benefits noted in mice models.[88] Results from a controlled trial in patients with hypertension noted that the frequency of aortic dissection was reduced in patients who were randomly assigned to receive valsartan compared with non-angiotensin II blockade (odds ratio 0·19, 95% CI 0·04–0·88).[89] These findings suggest that pathways that block angiotensin II can help to prevent aortic dissection. Repeat imaging at 1, 3, 6, and 12 months and then every year has been recommended.[36] Surgical repair has been recommended if maximum aortic diameter exceeds 5 cm (ascending aorta) or 6 cm (descending aorta), but the decision needs to take into account the risks of surgery in the individual patient.[36] Surgical risk will depend on the comorbidities of the patient, the extent of the procedure needed to achieve repair—eg, endovascular versus widespread aortic replacement and aortic branch revascularisation—and the estimated risk of aortic rupture or dissection. A family history of dissection, for example, has been suggested as a reason for intervention at a smaller aortic diameter.[90] Data from the IRAD emphasise that patients who have small-diameter aortas can also have aortic dissection; 40% of them have ascending aortas that measure less than 5·0 cm at presentation.[91] Patients (and their families) should be carefully instructed to maintain drug regimens, complete follow-up testing and visits, avoid sudden isometric exercises or activities that lead to thoracic trauma, and to have a strategy if recurrent symptoms develop.

Conclusions

Interest in aortic dissection has helped to fuel a large increase in our understanding of this condition over the past decade (panel 1). Improved understanding of connective-tissue diseases, such as Marfan's syndrome, is expected to lead to a range of new drug-based medical treatments that aim to slow aortic destruction and reduce the frequency of aortic dissection in these and other related conditions. Revolutionary techniques in molecular and genetic biology will hopefully also identify a range of targets for aortic dissection associated with other risk factors such as hypertension. The development of techniques and devices to deliver aortic repair via endovascular routes also promises to change acute and chronic management of patients after acute aortic dissection. Aortic dissection is still a highly lethal disease, which requires physician awareness and appropriate urgent management.

Conflict of interest statement

KAE has received unrestricted research grants for the International Registry of Aortic Dissection from the University of Michigan Faculty Group Practice, the Varbedian Fund for Aortic Research, the Mardigian Foundation, Biosite, and the University of Michigan Cardiovascular Center. KAE is a consultant to the National Institutes of Health's National Heart Lung and Blood Institute and Chairman of its GenTAC Registry (Genetically Triggered Aortic Diseases). JG declares that he has no conflict of interest.

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