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The Current Role of Intra-arterial Thrombolysis

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Background: *the role of intra arterial thrombolysis (IAT) in the management of peripheral vascular disease has come under scrutiny. This study aims to assess current usage and indications for IAT in the U.K.*
Method: *the use of IAT was assessed at our own centre and a questionnaire was sent to all centres that provide data for the U.K. "Thrombolysis Study Group".*
Results: *there has been a steady decline in the use of IAT at our centre from a peak of 40 cases per annum to zero. Response was received from 22 of 24 centres (92%). Nineteen (86%) reported a decline in IAT use. Main reasons were concerns over lack of efficacy (74%) and complication rate (63%). Most centres would use IAT for acute limb ischaemia (86%). However, for acute thrombosis in specific indications the results varied; synthetic graft (82%), vein graft (54%), supra-inguinal graft (54%) and thrombosed popliteal artery aneurysm (54%). When asked what their commonest usage for IAT was, the results again varied; acute limb ischaemia (40%), graft thrombosis (40%), embolism post radiological intervention (12%), other (8%).*
Conclusion: *there has been a significant decrease in IAT use. Concerns exist as to efficacy and complication rate. There is no clear consensus on indications.*

Key Words: Thrombolysis; Peripheral; Indication.

Introduction

From its inception by Dotter in 1974,[1] there was a gain in popularity for the use of intra arterial thrombolysis (IAT). In the U.K. IAT had a mixed reception. Difficulties with staff and high dependency bed availability hampered the adoption of IAT. Concern was expressed about complications, and also efficacy.[2] Many surgeons felt that cases suitable for IAT should be managed in specialist centres by experienced vascular surgeons.[3]

The aims of this paper are to assess whether IAT remains a popular treatment in the management of peripheral vascular disease and for what indications it is currently used in the U.K.

Methods

We reviewed the use of IAT at our own centre, where there are two vascular surgeons and three interventional radiologists serving a population of approximately 460 000. Numbers of episodes of thrombolysis were prospectively recorded. Annual rates were calculated.

To gain a national perspective, a questionnaire was sent to each of the centres participating in the U.K. "Thrombolysis Study Group". Established in 1992, this group comprises specialist vascular centres throughout the U.K. with an interest in IAT. Details from cases are centrally recorded on the National Audit of Thrombolysis for Acute Leg Ischaemia (NATALI) database.[4] With experience from over 1200 cases this group represents those centres in the U.K. that regularly use IAT.

To gain information about IAT use, each centre was asked: "Compared with 5–10 years ago, has your current practice of IAT increased, decreased or stayed the same?" "Can you give figures for; number of IAT procedures in 2001, maximum number that you undertook in a previous year?" "If the use of IAT has decreased, what are the reasons for this?"

To assess current practice of IAT, each centre was asked a series of questions (Fig. 1). They were also asked "What is the commonest indication for IAT in your unit at the moment?"

Data were collated on an Excel database (Microsoft Office 2000). Non-parametric data were analysed by Mann–Whitney test (Prism 2.01, Graftpad software).

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Would you use IAT in the following clinical situations?

		Always	*Sometimes*	*Rarely*	*Never*
Acute limb ischaemia	No neurosensory deficit				
	Some neurosensory deficit				
In a patient with claudication	Sudden worsening symptoms (days)				
	Worsening symptoms (weeks)				
Embolism following angiography					

Would you use IAT for the treatment of acute thrombosis of the following?

		Always	*Sometimes*	*Rarely*	*Never*
Popliteal aneurysm.					
Supra-inguinal graft					
Fem-pop bypass graft	Synthetic				
	Vein				
Fem-distal bypass graft	Synthetic				
	Vein				

Fig. 1. Questions asked to members of the Thrombolysis Study Group to assess their current practice of IAT.

Results

There has been a steady decline in the use of IAT in our unit (Fig. 2). From a peak of 40 cases per annum, no patient has undergone IAT in the last 2 years.

A response to the questionnaire was received from 22 of 24 centres (92%). A decline in the use of IAT was reported by 19 (86%). Three centres have maintained a steady level of IAT use (mean 32 limbs per year), representing 46% of all episodes of IAT in the whole group. No centre reported an increase in the use of IAT. In the last decade the total number of limbs undergoing IAT has decreased from a maximum of 367 in any one year to 210 in 2001. This represents an overall decrease in each centre from a median of 20 limbs per year (interquartile range 11–27) to 11 limbs per year (interquartile range 4–16) ($p = 0.01$).

In the 19 centres reporting a reduction in IAT use the reasons stated for this were concern about the lack of efficacy, either early (32%) or in the long-term (68%), and concern of the complication rate (63%). Lack of "back up" was considered a factor in half (47%) of those centres: This was specified as a lack of staffing in four (21%), lack of high dependency unit bed in five (26%) and lack of interventional radiologist availability

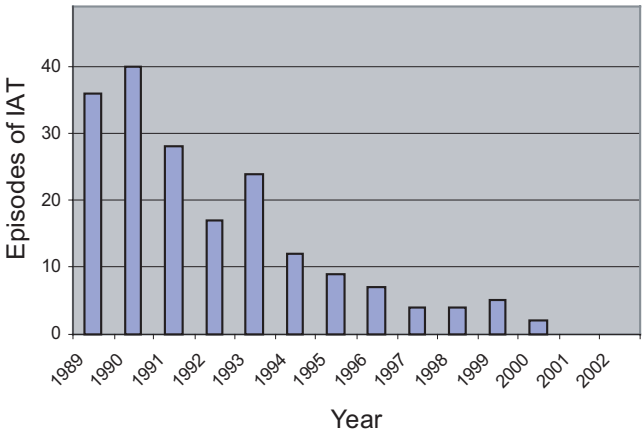

Fig. 2. Number of IAT episodes per year at our institution.

in five (26%). No centre reported that cost of IAT was applicable.

Currently most centres use IAT "always" or "sometimes" in cases of acute limb ischaemia (86%) and embolism following angiography (86%). Two centres "always" use IAT for acute embolism following angiography. For acute onset claudication most "never" or "rarely" use IAT (81%). Only one centre would use IAT "sometimes" for worsening claudication

Table 1. IAT use amongst centres in the Thrombolysis Study Group. Number of centres who would use IAT for acute limb ischaemia (ALI) with no neurosensory deficit or with deficit, a patient with claudication (IC) with sudden worsening symptoms (days) or worsening symptoms (weeks). Answers were graded "always", "sometimes", "rarely" or "never".

IAT use	Always	Sometimes	Rarely	Never
ALI	1	16	5	0
ALI (neurosensory deficit)	0	12	5	4
IC (days)	0	4	10	8
IC (weeks)	0	1	4	16

Table 2. Indication for IAT amongst centres in the Thrombolysis Study Group. Number of centres that would use IAT for acute thrombosis of; lower limb bypass graft (synthetic or vein)*, supra-inguinal graft, or popliteal artery aneurysm. Answers were graded "always", "sometimes", "rarely" or "never".

Indication	Always	Sometimes	Rarely	Never
Synthetic graft*	3	14	4	1
Vein graft*	2	10	9	1
Supra-inquinal graft	1	11	5	5
Popliteal artery aneurysm	1	11	8	2

* There was no difference between femoral-popliteal and femoral-distal bypass grafts so these responses are combined.

over weeks (Table 1). When asked about specific indications, there was no difference between femoral-popliteal and femoral-distal bypass grafts. Most (82%) would use IAT "always" or "sometimes" for acute thrombosis of a synthetic graft. This was lower (54%) for a vein graft. There was no clear consensus for IAT use in acute thrombosis of grafts above the inguinal ligament (54%) or for acute thrombosis of a popliteal artery aneurysm (54%) (Table 2).

When asked the commonest indication for IAT in their unit results were varied. The most common indications were graft occlusion (40%) and acute limb ischaemia (40%). Less common were embolism following angiography (12%), intra-operative use (4%) and in the upper limb (4%). In the three centres that did not report a decline in the use of IAT the most common indication was graft occlusion.

Discussion

There has been a steady decline in the use of IAT in our unit. This has not been matched by a rise in major amputation rate (unpublished data). This decline in IAT use is representative of a national trend within the U.K. "Thrombolysis Study Group" over the last decade. A few centres maintain the same level of use IAT, although this is the exception. The main reason for this decline was concern about the long-term efficacy. In theory IAT is an ideal treatment. Peripheral vascular disease progresses symptomatically in a stepwise manner due to thrombus formation on a pre-existing atherosclerotic lesion in the arterial vessel wall. To dissolve and disperse this thrombus by IAT would be extremely beneficial. However, in practice no significant benefits in terms of limb salvage or death at one year have been demonstrated from the use of IAT over surgery.[5] However, IAT use may reduce the extent of surgery or even the need for open surgery.[6–8] Recommendations suggest that IAT should be used in combination with other procedures, to define the underlying problem that is then treated either by angioplasty or surgery.[9]

In two thirds of centres concern about the complications of IAT were regarded as the main reason for fall in IAT usage. Main complications are intracranial haemorrhage (1–2%) and major haemorrhage (5–12%).[10,11] Risks are increased in the elderly.[12] Acute limb deterioration during thrombolysis can also happen.[7,13] It is interesting to note that a lack of "back up" remains an issue in these centres that have experience and have commonly used IAT. This figure remains unchanged from a previous survey in 1991.[2]

IAT remains popular for management of ALI without neurological deficit due to acute thrombosis. The role of IAT in worsening claudication is less popular and in keeping with the literature.[14,15] However, these results suggest that despite this, many would still on occasion use it. For worsening claudication over weeks most would never use IAT, an indication now obsolete.[16]

The response for IAT in management of acute graft thrombosis is varied and confusing. Initial results from our centre supported the role of IAT in the management of occluded bypass graft particularly in suprainguinal grafts.[17] Sub group analysis of the STILE data suggested a benefit but failed to reach statistical significance.[18] However, further analysis from the NATALI database revealed that patency on an intention to treat basis is approximately 20% at one year.[19] Despite this, graft thrombosis remains one of the most popular indications for IAT amongst the same group. The response for management of thrombosed popliteal artery aneurysm is mixed. This condition has a high rate of amputation and the use of IAT to salvage a limb may only delay revascularisation.[20] Those with demonstrable runoff should not undergo IAT.[9]

An interesting point from this trial is that despite results identifying those patients groups who do not benefit from IAT (elderly,[12] graft thrombosis[19] and IAT for acute worsening claudication[14]), centres are still

using IAT for these indications. Graft thrombosis being the most common indication particularly in the three centres that still commonly use IAT.

One of the main confusions about the indications for IAT has ironically been the STILE and TOPAS trials. These incorporated a heterogeneous mixture of cases. Patients with ALI or worsening claudication due to thrombosis or embolism occurring throughout the peripheral vascular system or in bypass grafts were all included and compared. There was no initial stratification by pathogenesis, location or symptoms. Subgroup analysis was consequently flawed by small numbers, either directly in the trial or combined with others after meta-analyses.[5,21] Despite this a small subgroup of patients (10–30%) in these and subsequent trials underwent IAT with good results, without complications and requiring no further intervention. The question remains who these are and how they can be identified.

Current roles that remain to be analysed for IAT are embolism following intervention and intraoperatively to clear smaller vessels following failed embolectomy. These represent small patient numbers. The role of IAT in the management of ALI due to native vessel thrombosis remains to be assessed. Acute leg ischaemia (ALI) leads to a high patient mortality and morbidity. Early attempts to address this centred on presenting features by stratifying the cases as viable, threatened or non-viable.[22] The appropriate operation and timing for surgery was shown to reduce the mortality and need for subsequent operations.[23] More recently the use of P-POSSUM scoring to assess patients prior to IAT has been predictive of outcome.[24] Have we now come full circle after the initial enthusiasm?

Conclusion

In the last decade there has been a significant decrease in the use of IAT in the U.K. Thrombolysis Study Group. Concerns exist as to the efficacy and complication rate. Of those still using IAT acute limb ischaemia and graft thrombosis are the most common indications.

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