ADM-assisted Implant based breast reconstruction vs Free tissue transfer breast reconstruction

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3 part questions:

Patient characteristics:	In post mastectomy patients
Intervention question:	Free tissue transfer based reconstruction or ADM+implant breast reconstruction
Relevant outcome:	Yield better patient satisfaction, risk-effectiveness ratio and cost effectiveness

Introduction

Despite in the recent decade, the free tissue transfer has been the gold standard for breast reconstruction and evolving of DIEP, TUG flaps to e the most common used breast reconstruction approach at present time, however the complexity of the procedure, long operative time, donor site comorbidities, long learning curve and subsequently increased cost were always present as downside of this approach.

More recently with the advances in tissue engineering, the development of Acellular Dermal Matrix variants provided better implant coverage, more aesthetically pleasant lower pole outcome and, alleged, less post radiotherapy complications. With addressing these previously notorious concerns resulted in shifting away from implant based breast reconstruction in the past, now the implant based reconstruction is back in the race.

In this review, we are trying to highlight the evidence supporting using either the Free tissue transfer vs ADM-assisted implant based approaches for breast reconstruction in terms of patient satisfaction, risk-effectiveness ratio and cost.

Clinical scenario:

A 56 years old female is undergoing a skin sparing mastectomy for breast cancer with expected postoperative radiotherapy, will a free tissue transfer e.g., DIEP breast reconstruction or Implant based +ADM breast reconstruction yield a better outcome in terms of patient satisfaction, cost effictiveness and risks?

Search strategy:

Medline 2008-April 2018 using the pubmed interface

[(exp Breast reconstruction) AND ADM AND Implant

LIMIT to English.

Search outcome:

141 papers were found.

Of which 121 publications in the last 5 years , only 61 were relative to humans.

of these were excluded as they were non relevant to the reconstructive approach.

Remaining 19 publications were included.

Relevant papers:

	Author, date and country	Patient group	Outcomes	Key results
1	Martin L 2013 May UK	Joint Guidelines of ABS/BAPRAS	ADM does not increase the risk of post radiotherapy capsular contracture (4 folds), and might decrease this risk.	ADM is indicated in: Planned immediate IBBR Alternative to 2 staged IBBR Mastectomy weight of >600gms Adequate skin envelope
	Sbitany H[1].	Post mastectomy	Use of ADM has enhanced the	Reduced risk of

2	2017 Dec USA	Breast Reconstruction	aesthetics and outcome	capsular contracture rates Better aesthetic definition, implant coverage and soft tissue support
3	Apte A 2016 Jan UK	53 One stage ADM-assisted IBBR	Patient Reported Outcome Measures (PROMs) : 1.7 days mean hospital stay post-surgery. 93.3% high level of body confidence 6.7% post-surgery pain Return to light activity in 2.5 weeks and full activity 5.4 weeks	ADM-assisted IBBR shows high level of cosmetic satisfaction, shorter recovery and low incidence of post-operative pain
4	Kankam HKN et al 2018 Jan UK	137 implant only reconstruction vs 127 implant +ADM RECONSTRUCTION	Increase of Implant based reconstruction with ADM from 16% to 52% of all breast reconstruction compared to decrease of DIEP and LD approach No difference of early complications rates with or without ADM	Introducing ADM has shifted the breast reconstruction approach to implant based to replace the more complicated and expensive autologous techniques
5	Tran BNN et al 2017 Sept. USA	TE/I+ADM cost vs DIEP cost (including complications cost)	$13 304.55 TE/I+ADM $10 237.13 DIEP Including complications: $13 963.46 TE/I+ADM $12 624.29 DIEP	DIEP has lower cost compared to two staged TE/I+ADM approach
6	Krishnan NM 2014 April USA	Comprehensive literature review was carried out for complications of two staged IBBR to determine the cost effectiveness of ADM usage vs IBBR without using the ADM	30% complications rate with ADM 34.5% complications rate without ADM Base cost increase of $361.96 with using the ADM. Increased of Quality Adjusted Life Years with ADM is 1.37	Despite increased cost, ADM usage in 2 staged IBBR is cost effictive
7	Hunsicker LM 2017 Jan. USA	1584 ADM-assisted direct to implant one stage operations	Complications rate comparable to 2 staged IBBR	One stage ADM-assisted IBBR is a safe, reliable and effective approach with comparable complications rate to 2 staged approach
	Chopra K 2017 April	Post mastectomy with 2 staged	Biopsies from ADM adjacent tissue showed less thick capsule	Using ADM in the first stage of 2

8	USA	IBBR+ADM	compared to pectoral adjacent tissue	staged IBBR reduced the thickness and inflammatory character of the capsule
9	Headon H 2016 June UK	118 post SSM with IBR+ADM(SURGIMEND)	PATIENT SATISFACTION 9/10 Capsular contracture 2.9/10	ADM(SurgiMend) in IBBR has high patient satisfaction rate and very low inflammatory reaction. Neither prior radiotherapy nor post-operative radiotherapy are contraindications to using it.
10	Yu D et al 2016 May USA	24 ADM capsules vs 24 non-ADM capsules histologically analysed	Significantly less vascular proliferation in the ADM capsule.	Decreased inflammatory response and capsular contracture in the ADM IBBR
11	Lee KT 2016 Feb. South Korea	Meta-analysis of studies comparing submascular traditional IBBR to ADM IBBR 2011-2014(6199 cases)	The use of ADM increased the risks of infection, seroma and skin necrosis. The use of ADM decreased the risk of capsular contracture and implant malposition. ADM allowed greater expansion	Over all morbidity related to ADM use is not remarkable ADM benefits of reducing late complications and improving implant dynamics are appreciable.
12	Ibrahim AM June 2015 USA	5 Independent blinded plastic surgeons objectively reviewed pre and post-operative photos of 20 TE/I IBBR vs 18 TE/I+ADM IBBR for cosmetic outcome	ADM improved: breast contour, lower pole projection, implant placement and inframammary fold definition	ADM-assisted IBBR is aesthetically superior to non ADM-assisted IBBR
13	Forsberg CG 2014 USA	18 blinded evaluators scored the cosmetic appearance of post-operative photographs from 1 to 5 in patients had IBBR.	ADM group showed higher infection rate , lower capsular contracture rate and better contour, symmetry and aesthetic appearance	The use of ADM in IBBR confer a significant advantage in aesthetic outcome and capsular contracture risk reduction with a

		Total of 183, 58 ADM-assisted and 125 traditional submuscular reconstruction		higher risk of infection

Comment:

Breast reconstruction has been evolving fast for the past few decades. Recently the free tissue transfer has been the gold standard in Breast reconstruction replacing the Implant based breast reconstruction (IBBR) in most of the world, providing reliable, autologous, safe and, most importantly, durable tissue that handles the common peri-operative radiotherapy reliably.

However, with the recent advances in tissue engineering and the wide spread of the Acellular Dermal Matrix (ADM) has revolutionized the breast reconstruction and put the IBBR back to the race side by side with the free tissue transfer.

Where some units have adopted the ADM-assisted IBBR either one stage or two staged approaches, other units raised relevant questions with regards to the ADM-assisted IBBR.

Despite having shorter theatre time, hence less cost, the ADM added cost was a concern. The notorious ADM related early post-operative complications e.g. infection, seroma, implant loss and theatre revisits were concerns to be investigated. The claimed evidence of reducing the capsule contracture is another question to be answered. The cosmetic benefit especially in lower pole, implant coverage and contour enhancing are other factors to be highlighted.

In this systematic review, we try to collect the available evidence to address these concerns to try to find a clear answer whether the ADM-assisted IBBR is a safe and reliable breast approach the the validated above mentioned benefits which top the more complicated, lengthy, costly and demanding free tissue transfer or still the downsides of the ADM-assisted IBBR outweighs its merits.

In 2013 Martin L et al at Aintree published ADM guidelines in BAPRAS trying to regulate the new wild horse emerging widely in the breast reconstruction(1).Clear and relative indications plus precautions based on the limited data available that time, gave the green light for the ADM to be used in a more systematic way and resulted in more data available at present time enables us to have more guidance when considering using the ADM.

The Safety of using ADM has been always a concern due to the claimed increased risk of complications e.g. seroma, infection, skin necrosis, theatre revisits and implant loss. In 2016 Lee KT et al performed a meta-analysis concluding 6199 cases comparing the traditional submuscular implant reconstruction with ADM-assisted approach(11). They reported higher

risk of early post-operative morbidities including seroma and infection. However they did not find remarkable difference compared to the traditional ADM-free approach. Krishnan NM et al(6), in 2014, when performed a comprehensive literature review comparing the 2 staged IBBR with and without ADM in terms of post-operative complications and found that ADM-assisted IBBR had 30% complications rate compared to 34.5% in IBBR without ADM.

The added benefit of cosmetically enhancing the reconstructed breast with ADM especially with lack of breast tissue after mastectomy and lower pole augmentation plus allowing better expansion was validated by the work of Ibrahim AM et al in 2015(12). They had 5 independent blinded plastic surgeon reviewing the pre and post-operative photographs of two staged IBBR with and without ADM from cosmetic outcome angle. They have concluded that ADM-assisted IBBR had improved contour, lower pole projection, infra mammary fold definition and implant placement. This great work came in agreement with their successor Forsberg CG et al (13)in 2014 who had 18 blinded reviewer scoring 183 breast reconstruction from 1 to 5, being 5 is the most cosmetically appealing reconstruction. They have concluded that the ADM-assisted IBBR group had a better cosmetically appealing outcome in terms of contour, symmetry and implant position. Moreover Apte et al in 2016 (3) reported 93.3% high level of body confidence in 53 cases of ADM-assisted IBBR.

Another major concern was the capsule contracture, especially with common post-operative radiotherapy which enabled the autologous free tissue transfer to claim the golden medal for the most reliable reconstruction approach in such condition and the notorious reputation of capsule contracture in IBBR which has a 4 folds risk increase with radiotherapy. Chopra K et al in 2017(8) had an interesting study when they took two biopsies at the time of replacing the expander with implant from the pectoral adjacent capsule and the ADM adjacent capsule. The results showed, clearly, that the ADM capsule had thinner capsule with less inflammatory response. This confirmed the work of Yu D et al in 2016(10) when they analysed histologically 24 ADM capsules vs non ADM IBBR capsules and found that ADM-assisted IBBR capsules show significantly less vascular proliferation and concluded that it has less risk of capsule contracture.

On the other hand, a key factor in considering recruiting a management approach is cost effectiveness. This particular point was a fierce debate between two teams. The ADM supporters claimed that due to much shorter theatre time, less complicated equipment and quicker learning curve the ADM is more cost effective. Paradoxically the Autologous free tissue transfer team thought the added cost of the ADM plus the alleged risk of theatre revisits could mean that ADM is not a cost effective option. In 2017, Tran BNN et al(5) compared the cost of two staged IBBR to DIEP as the most common autologous free tissue transfer used in breast reconstruction. Using the reimbursement codes, they found that the average cost of DIEP is $10 237.13 compared to $13 304.55, in case of 2 staged IBBR . They added the average complications cost and this demonstrated that two staged IBBR cost is $13 963.46 compared to $12 624.29 for the DIEP. Despite the cost was not significantly different, however the comparison was to a two stage ADM-assisted IBBR approach. This could be significantly lower in case of adoption of the one stage approach which was found reliable through the work of Hunsicker LM et al in 2017 (7)when they reviewed the complications rate of 1584 one stage ADM-assisted IBBR and found that it is comparable to the two stage approach. Apte A et al in 2016 (3)added more credit to cost effectiveness the one stage ADM-assisted IBBR, when they reviewed the hospital stay and return to activity duration in 53 cases and reported mean hospital stay of 1.7 days post-surgery

and 2.5 weeks return to light activity and 5.4 weeks to normal activity. Compared to the longer hospital stay (5-7 days post-surgery) and delayed return to activity mainly due to donor site morbidity and chest wall operative insult. These factors conclude that,, in fact, the one stage ADM-assisted IBBR could be cost effective approach of choice.

It was not a surprise that Kankam HKN et al in January 2018(4) reported that in 264 patients over the last 18 months the ADM-assisted IBBR percentage has increased from 16% to 52% of all breast reconstruction procedures, stepping down the DIEP from 49% to 34%. Which can be a sign of a pending shift in the breast reconstruction in the following years.

Clinical bottom line:

The available data suggest that ADM-assisted IBBR has unremarkable higher rate of early postoperative complications, however it enhances the cosmetic outcome and patient satisfactions. Moreover there is some evidence that it could represent a more cost effective option compared to the autologous free tissue transfer.

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