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Use of Negative Pressure Wound Therapy in Treatment of Enteroatmospheric Fistulas: Critical Review of the Literature

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***Abstract* - There are a few situations in surgery as challenging as management of open abdomen (OA). Probably the worst and most devastating complication of OA is an exposed (enteroatmospheric) fistula. Such patients have high mortality and morbidity rates. Mortality rates in patients with gastrointestinal fistula is 5-20% increasing up to 66% in the setting of OA. The most important factor attributable to such high mortality rates is septic response to bacterial burden arising from stool content in the open wound. Surgical closure of the fistula is scarcely successful and diversion of the enteral content by means of standard wound care options is ineffective and insufficient. Introduction of novel wound treatment options such as negative pressure wound therapy (NPWT) opened new horizons in the management of OA and its complications. Up to this date no method was accepted as a standard, rather, all of them bear signs of improvisation and creativity. Authors in the article reviewed available up-to-date literature confronting it with their own experiences with the aim of aggregation of information, comparing the methods, and finding the most feasible method and direction for future development of NPWT in treatment of enteroatmospheric fistulas in OA.**

Keywords — **negative pressure wound therapy – vacuum therapy – open abdomen – enteroatmospheric fistula**.

I. Introduction

Despite recent medical advances, the management of gastrointestinal fistula pose a significant challenge and carries mortality rates ranging from 5-20% [1,2]. In the setting of open abdomen (OA) the mortality rates increased up to 66% [3,4]. This situation represents grade III or grade IV open abdomen classification by Björck [5]. Presence of enteroatmospheric fistula in OA is considered probably the worst and most devastating complication of OA [1].

Fistulas are defined as abnormal communication between two epithelized surfaces with several classifications used for their description [6,7]. Anatomic classification names the fistulas according to organs involved while high pressure organs from which fistulas arise is named first. Since open abdomen does not fall under such classification and fistulas in OA have no overlying tissue, they are classified as enteroatmospheric [1,8]. Another classification of fistulas is based on 24 hour output. High output fistulas produce more than 500 ml/24 hours, moderate output 200-500 ml/24 hours, low output produce less than 200 ml/24 hours. Debate over correlation between the volume and fistula output can be observed in the literature [6,9]. Our belief is that successful closure of the fistula is directly attributed to volume produced.

Fistulas typically occur in postoperative periods following surgery for cancer, ileus, or complications of inflammatory bowel diseases (IBD) [10]. Other causes include shear stress of the bowels in reoperations and in redresses in management of OA. The most important factor attributable to high mortality rate in the setting of open abdomen is septic response to bacterial burden arising from the presence of stool content in the open wound. Production of the stool into the wound is permanent and standard wound and stoma care is ineffective in diversion of enteral content from the wound.

The treatment is demanding from the side of medical personnel, patient and family, is expensive and of long duration. It encompasses a wide and multidisciplinary approach with attention to sepsis control, organ support, nutritional care and wound management. Specialists involved include surgeons, intensive therapy specialists, anesthesiologists, radiologists, clinical microbiologists, nutritional specialists, psychiatrists, internists, nurses and wound therapy experts. Patients with OA pose a considerable economic burden on healthcare provider complicating systemic centralization of the patients in one institution.

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Management of patients with intestinal fistulas can be guided my "SNAP" acronym. "S" stands for sepsis and skin care, "N" for nutrition, which is ideal to be administered enterally. "A" stands for diagnosis of underlying anatomy (height of the fistula) and "P" for definite plan to deal with the fistula [11]. Nevertheless, there is vast difference in management of enterocutaneous fistulas and enteroatmospheric fistulas. This is due to inadequacy of the overlying tissue, which by overgranulation serves as a part of the closure mechanism, as well as sepsis resulting from spillage of enteral contents in the open wound. While majority of enterocutaneous fistulas will respond to conservative management and will close in 6 weeks [12], opposite is true of enteroatmospheric fistulas.

Systemic treatment of sepsis, delivery of adequate nutrition and organ support, including circulatory, respiratory and renal support together with pain management and thromboembolic prophylaxis, are aspects that cannot be sufficiently stressed, and without these any surgical or conservative procedure for fistula management is destined to failure.

Mathematical models show the influence of increased intestinal pressure in reluctance of primary healing of the fistula [13]. Thus, decompression medication is recommended. The role of sandostatin delivery still has to be stated.

Surgical closure of fistula is scarcely successful and diversion of the enteral content by means of standard wound care options is ineffective and insufficient, leading to further worsening of the patients clinical state. Surgical intervention and resection with reconstruction/stoma creation in such patients carries high risk of perioperative complications with high probability of creation of another fistula when handling edematous, inflamed and paralytic bowels in the setting of catabolism and sepsis. Nevertheless some authors advocate this tactic changing impossible to improbable [14].

Introduction of novel wound treatment options such as negative pressure wound therapy (NPWT) opened new horizons in management of OA and its complications. Up to this date no method was accepted as a standard, rather all of them bear signs of improvisation and creativity of medical personnel.

II. Methods

Authors performed a literature search through Web of Knowledge[sm] (Thomson Reuters) including Web of Science® (Science Citation Index Expanded (SCI-E), Social Science Citation index (SSCI), Conference Proceedings Citation Index - Science (CPCI-S), Conference Proceedings Citation Index - Social Sciences & Humanities (CPCI-SSH), Book Citation Index– Science (BKCI-S), Book Citation Index– Social Sciences & Humanities (BKCI-SSH)), BIOSIS Citation Index[SM], Current Contents Connect®, MEDLINE®, Journal Citation Reports®, and Scopus®. Search terms were combination of phrases: "open abdomen", "enteroatmospheric fistula", "negative pressure wound therapy", and "vacuum assisted closure".

All results were processed with search for articles, where specific method of use of negative pressure on enteroatmospheric fistula was described. Identified articles were further analyzed in terms on number of patients, methods used, closure of fistula, time to closure and mortality.

III. Results

After performing the literature search and identifying articles where specific methods of use of NPWT on enteroatmospheric fistula was described, we found 18 literature works [2,3, 15-30]. These papers are summarized in table 1.

All of these papers state the presence of enteroatmospheric fistulas as being a grave complication of open abdomen, with great impact on morbidity and mortality. Based on these works, two main treatment pathways can be chosen.

First is the aim for primary resection of the fistula [14] with preoperative or postoperative application of NPWT for prevention of complications [21]. This approach, however, carries a risk of an inflammatory response from the patient, who is usually in a catabolic and septic state, often with multiple organ dysfunction or failure.

Another approach is to primarily aim for controlling the enteral content by use of NPWT. The rationale is, that by diversion of enteral content from the open wound we promote systemic improvement, elimination of sepsis, improvement of nutritional status and after a defined time (usually 3-6 months), patients will undergo a secondary operation with reconstruction of the gastrointestinal tract.

Primary closure of the fistula is very rare, seldom successful with sutures or glue [2,23]. NPWT might be of help either by primary application [18,30] or by use of a muscular flap secured by NPWT [20,29].

IV. Discussion

There are few situations in surgery as challenging as the management of an open abdomen (OA). The treatment is demanding from the side of medical personnel, patient and family, is expensive and of long duration. Probably the worst and most devastating complication of OA is an exposed (enteroatmospheric) fistula [1]. Such patients have high mortality and morbidity rates. Mortality rates in patients with gastrointestinal fistula is 5-20%[2] increasing up to 66% in the setting of OA [3,4]. The most important factor attributable to such a high mortality rate is the septic response to bacterial burden arising from stool contents in an open wound.

Introduction of novel wound treatment options such as negative pressure wound therapy (NPWT) opened new horizons in the management of OA and its complications.

Treatment of the fistulas today goes by the SNAP acronym (sepsis and skin management, nutrition, anatomy of the fistula, definite plan). Two main approaches can be taken, surgical resection of the fistula and its closure, or conservative treatment. Conservative treatment is said to be successful in most of the cases and majority of the fistulas will close in 6 weeks [12]. This, unfortunately, can be attributed only to fistulas, which do not cause further septic response of the patient with concomitant catabolism and organ dysfunction. If a fistula does not have overlying tissue, the chance for spontaneous closure dramatically decreases. Typical situations of such a fistula are seen in an enteroatmospheric fistula into the open abdomen, with its effluent causing systemic inflammatory reactions. In such cases wound management and effluent control is by standard means

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insufficient and unsuccessful, leading to further development of sepsis and increased mortality rates. Resection or anteposition of the bowel with stoma creation can be considered in such patients "a salvage operation" switching the chance of survival from impossible to improbable. It is important to note, that the economic burden of these patients is high and treatment is demanding from the side of the medical personnel as well as family members and the patient themselves.

Use of negative pressure wound therapy further widens the horizon for the treatment of enteroatmospheric fistulas. Firstly, its use on fistulas was considered a contraindication of use; recently it is being accepted and in multiple studies is showing its effect. There are references in the literature suggesting association of fistulas with use of NPWT [31] but in larger studies no such association was proven [25,32].

Economic burdens place pressure on the rational for use of NPWT with creation of standards on one side, reluctance of accepting and gathering such patients in one institution on the other side. NPWT as a relatively new method in use in management of OA and its complications does not have a standard algorithm and even current recommendations accept and work with "out of recommended indications" use of NPWT [33].

Possible usage of NPWT in treatment of enteroatmospheric fistulas can be divided into a couple of approaches.

Primary closure of the fistula would be the most desirable situation. Primary sutures and use of fibrin glue on the fistula was described, but with "anecdotal success" [2]. However, use of PVA (polyvinyl alcohol) foam on the mouth of the fistula without eversion of the mucosa was in our experiences and also in reviewed articles in most cases successful [27,30]. Another possibility is coverage of the fistula with muscular flap, usually m. rectus abdominis, with its fixation with NPWT or even covered with split-skin graft as a "parachute" [20,29].

If primary closure is not feasible, the goal is diversion of the effluent outside from the wound. The rationale is to close the wound, improve the systemic state of the patient, convert from NPWT to stoma care of the fistula, and after 3-6 months perform secondary surgical reconstruction.

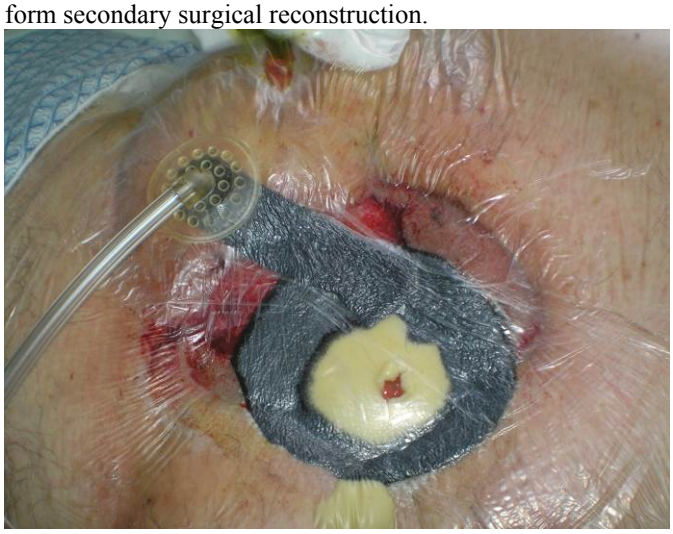

Fig 1: Fistula diversion sec. Govermann (own material M. Hutan)

The first such technique was described by Govermann [17], where the visceral block is protected by Xeroform, fistula mouth bordered with foam and diverted outside of the wound into the stoma bag. Use of stoma paste in such diversion facilitates its feasibility and successful application [30]. Another possibility of diversion was described by Al-Khoury. Diversion is performed by insertion of Malecot catheters into the mouth of the fistula, covering the rest of the wound with NPWT, bringing the catheters outside of the wound [34]. Another possibility was described by Stremitzer and Banasiewicz, where mouth of the fistula is controlled by one negative pressure device (with or without use of Jackson Pratt drain and placing a cone shaped foam over it), the rest of the wound is controlled by a second NPWT device [26,28].

More devices are known to be used for content diversion, including different tubes, endotracheal cannulas, baby suckers or even newly launched industrial products.

All of these options can be used, if the mouth of the fistula is easily accessed and the distance of it from the anticipated ventral abdominal wall is as little as possible. In cases, when the fistula is not easily accessible or the effluent is of another attribute (bile, pancreatic juice), only direct application of NPWT is recommended. Any use of catheter intubation devices in deep fistulas will not only enlarge the mouth of the fistula, but they will surely be unable to control the secretion from the fistula [35]. Use of direct application of NPWT will enhance the wounds characteristics and can prepare the patient for surgical resection [21]. Although not an ideal approach, its use with success is described repeatedly in the literature [2,3,16].

V. Conclusion

Enteroatmospheric fistulas in open abdomen remain the most devastating complication with great impact on morbidity and mortality. The treatment is demanding from the side of medical personnel, patient and family, is expensive and of long duration.

Introduction of new wound treatment options like NPWT enables new way of its management. Although mostly desirable, primary closure of the fistula is rare, but if the mucosa is not everted, feasible with NPWT. The best option of management seems to be diversion of the enteral contents outside of the wound by means of one of three presented methods (Govermann, Al-Khoury, Stremitzer). If such possibility is not possible, the only possibility is direct application of negative pressure into the wound.

The aim is getting the patient out from sepsis, improving his systemic status, enhancing their nutritional state, and planning elective surgical reconstruction in 3-6 months.

Use of muscular flaps for primary closure of fistulas is an interesting concept, which, due to small amount of patients presented in the literature, requires further work.

No studies comparing such methods were performed and by our opinion, research and patient data gathering is essential for further development of strategies, which would decrease the mortality and morbidity rates in patients with this devastating complication. Until the creation of an algorithm, treatment

stays on patient-by-patient decision of the surgeon with wide interdisciplinary team of medical practitioners.

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Author, year	No of patie-nts	Types of fistula	Method used	Spontane-ous closure of fistula	Succesful manage-ment of fistula	Time for fistula closure	Mortal-ity rate	Conclusion/Remarks
Alvarez et al, 2001	1	sigmoid, prox-imal jejunum, distal ileum	direct appli-cation of NPWT	1 (100%)	1 (100%)	2 months	0%	NPWT is an effective tool with important implication for cuta-neous GI fistula man-agement
Cro et al, 2002	3	small intestine	direct appli-cation of NPWT	2 (66%)	3 (100%)	3 wks -5 m.	0%	All fistulas were high output (over 1 l/24 hrs), one treated with surgery after reduc-tion of output to 200 ml/24 hours after 4 months. NPWT ap-plied for 3-5 wks
Goverman et al, 2006	5	enteral fistulae	diversion of the stool into the stoma bag, sepa-rated from black foam by xeroform	0%	5 (100%)	6 - 10 months	40%	Primary approach to divert the content, bring the patient from sepsis, do the split skin grafting and months later undergo elective surgery with resection of fistula, reanastomosis and repair of hernia wall with prosthesis
Draus et al, 2006	13	small intestine, colon, stomach, duodenum	direct appli-cation of NPWT	1 (7,7%)	13 (100%)	12 wks - 6 months	0%	One patient with suc-cessful primary clo-sure of fistula, other needed surgical in-tervention. In all pa-tients NPWT im-proved the condition of the wound, in some promoted wound contracture and heal-ing.
Gunn et al, 2006	15	enteral fistulae	direct appli-cation of NPWT	11 (73,3%)	15 (100%)	primary avrg 14 days	0%	Primary closure was seen in patients with no visible intestinal mucosa on examina-tion pointing to con-clusion, that presence or absence of visible mucosa is the single clinical most im-portant factor for use of NPWT on fistula.

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Denzinger et al, 2007	1	ureoileal anastomotic leakage	NPWT tube covered with foam and Mepithel, inserted into the fistula canal	1 (100%)	1 (100%)	32 days	0%	Patient with urothelial ca, after cystectomy and op sec. Bricker, leakage from anastomosis into open abdominal wound.
De Weerd et al, 2007	1	enteral fistula	latissimus dorsi/m. serratus flap with inter-position of NPWT	1 (100%)	1 (100%)	N/A	0%	Use of muscular flap for cover-age of abdominal wall defect and mouth of fistula - descrip-tion of a novel approach.
Rao et al, 2007	6	enteral fistula	intraabdomi nal dressing set	0 (0%)	2 (33,4%)	N/A	66,70 %	Patiens with OA managed by NPWT, according to authors, caution has to be taken when indicating NPWT in presence of bowel anastomosis or enterotomy repair.
Dionigi et al, 2008	13	ileum in 80%	direct ap-plication in preparation for surgical reection	0 (0%)	13	N/A	21%	Primary treatment of patients was by resection of fistula, VAC was used preoperatively for preparation and wound man-agement (7 patients) and postoperatively to prevent complications (6 patients).
Al Khoury et al, 2008	3	N/A	Malecot catheter in fistula and NPWT around	0 (0%)	3 (100%)	N/A	N/A	Authors describe method of fistula control by insertion of Malecot catheter into the mouth of fistula and direct application of NPWT in the open abdomen.
Horwood et al, 2009	2	N/A	surgical resection in adjunct to NPWT	0 (0%)	2 (100%)	N/A	0%	Authors describe series of 27 patients with OA treated by NPWT, in 2 fistula formation, one was sutured during re-operation, second one was resected with successfull re-sults.
Ruiz López et al, 2009	3	N/A	surgical resection in 1, fistula VAC sec. Al Khoury in 2	0 (0%)	3 (100%)	N/A	2 (66%)	Authors describe improvement of wound characteristics and good fistula control, two deaths were 5 weeks and 2 months after the procedure due to cardiac failure and pneumonia.
Shaikh et al, 2010	2	ileum	direct ap-plication and surgical manage-ment	0 (0%)	2 (100%)	N/A	0%	One fistula in distal ileum was stapled and ileostomy created, second patient with multiple fistulas was managed with di-rect application. Both patients were elecively reconstructed in later time.
Stremitzer et al, 2011	9	enteral fistu-lae	targeted drainage of fistula with cone shaped foam	0 (0%)	8 (89%)	surgical after 3 months	11%	Authors present a method, where Jackson Pratt drain is inserted in the fistula, cone shaped foam and suction is placed over it, regular NPWT is in the rest of the wound, aim is elective surgical management after 3 months.

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D´Hondt et al, 2011	9	small intestine	direct coverage with PVA in small, diversion sec. Govermann in large	3 (33%)	9 (100%)	12 - 52 days	11%	Authors propose use of direct coverage of small fistulas with PVA foam for primary closure and divert content from large fistulas with latter surgical resection afte 6-10 weeks.
Banasiewicz et al, 2011	3	enteral fstulae	bridging with targeted drainage, preparation for surgery	0 (0%)	3 (100%)	3 wks - 6 months	0%	Authors propose diversion by use of targeted drainage with subsequent surgical reconstruction after improvement of patients clinical state (not sooner that 3-5 weeks though)
De Weerd et al, 2012	1	jejunum	parachute design (coverage with muscular flap and NPWT)	1 (100%)	1 (100%)	N/A	0%	Initial treatment with coverage of fistula with m. rectus abd. flap sutured to fistula, covered with split skin graft and NPWT.
Hutan et al, 2013	9	enteral fistulae	direct coverage with PVA in small, diversion sec. Govermann in large	1 (11%)	7 (77%)	N/A	37% in whole group	Authors propose use of direct coverage of small fistulas with PVA foam for primary closure and divert content from large fistulas with eventual latter surgical resection afte 6-10 weeks.