Negative Pressure Wound Therapy – Our Experience in a Secondary Level Care Hospital

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I. INTRODUCTION

Wound closure is one of the most important end points in surgical practice. Surgically created wounds are mostly planned in such a way so that wound closure does not involve much effort. Even in cases of surgical site infections, the skin cover can be achieved in most of the cases. In cases of extensive tissue loss, exposed bone and tendon surfaces, deep deformed wounds like necrotizing soft tissue infection or post traumatic wounds, special efforts or additional surgical procedures may be required to achieve viable skin cover. A successful wound closure should essentially cover all the bony and muscular surfaces with a stable skin cover without affecting the primary function of that particular part of body.

The history of Negative Pressure Wound Therapy (NPWT) [1] dates back to 18th century when lip suction was one of the modalities of wound management. It involved the basics of modern NPWT-suction of exudates and harmful matter (debris) thus providing a conducive environment for wound healing. Subsequently glass leech model and cupping was used predominantly in 19th century as a modification of the therapy. However significant progress was made towards the end of 20th century after the advent of foam dressings. In 1990s Dr Louis Argenta and Michael Morykwis [2] first time, demonstrated the use of modern NPWT in the form of Polyurethane Foam with mechanical vacuum. Since then, it has been extensively used as an effective method for managing complex wounds mainly due to its different mechanisms of action in different clinical situations that include perfusion changes, micro-deformation, macro-deformation, exudates control, decrease in bacterial load, etc to name a few. [3]

II. AIM AND OBJECTIVE

The purpose of this study is to analyze the effect of Negative Pressure Wound therapy (NPWT) on healing of wounds over a period of 02 years.

In addition, the versatility of NPWT and its successful application on few rare cases of non-healing ulcers as well as its relevant literature are reviewed.

III. MATERIALS AND METHODS

This is an observational, retrospective study, designed to analyze the effect of NPWT in various types of wounds in the General Surgery department of a secondary level care hospital in India over a period of 02 years from Jan 2020 to Dec 2021.

Inclusion criteria

(a) Patients more than 18 years of age

(b) Wounds greater than 16cm² surface area

(c) Depth of the wound included full thickness skin loss with or without damage to subcutaneous tissue, muscle, tendon or bone underneath

(d) All such wounds that could not be closed primarily or secondarily irrespective of size.

(e) Confirmed adequate blood supply to the wound and the surrounding area (clinically or by duplex imaging)

Exclusion criteria

- (a) Wounds with active infection, slough, necrosis and / or purulent discharge
- (b) Wounds with active / ongoing bleed
- (c) Ulcers / gangrene due to vascular aetiology like PAOD (excluded after arterial Doppler study).
- (d) Patients with known allergies to foam / components of NPWT systems
- (e) Unwilling patients
- (f) Patients who developed permanent leak in NPWT seal during the treatment process

NPWT Equipment

Standard equipment of Acti V.A.C. ® NPWT System, Kinetic Concepts Inc. (KCI) [4] which is able to produce negative pressure ranging from -25 to -200 mm Hg and achieve vacuum seal using polyurethane foam along with plastic, adherent, skin friendly tapes were used in all the patients. It consists of a replaceable canister for collection of debris and standard connective tubing. In our study, all the wounds were treated with negative pressure between -75 and -125 mm Hg as recommended by various studies using this equipment. NPWT was given for a period of 03-05 days in one sitting. Several patients required two or more sittings of NPWT before being taken up for definitive wound closure. All patients were advised regarding restriction of movement and maintenance of seal to avoid inadvertent leakage. Ward staff were instructed to monitor the maintenance of negative pressure at set level (between -75 and -125 mm Hg) and report in case of leak / obstruction alarm. [5]

The wounds were assessed prior to application of the NPWT in terms of depth, size, and absence of necrotic material, exposed bone or tendon. Wounds were reassessed after removal of NPWT as per the same parameters. Difference in size and wound bed cover using standard measurement tools (Derma Map Overlay-Grid based measurement of wound outline and Scaled swab stick for wound depth, length and breadth) was noted after each removal of NPWT. Bates Jensen Wound Assessment tool was used as a guiding factor for assessment of wounds. [6] Appearance of healthy pink granulation tissue all over the wound surface was considered as success of NPWT and it was used as deciding factor for consideration of other forms of wound closure like secondary suturing of split skin grafting and so on. The wound closure was defined as complete cover of the wound by healthy and viable skin (which could be by secondary closure by approximating the edges, split skin graft or flap cover as per the clinical condition). Complicated wounds that required specialized grafts or flap cover for wound closure were referred to tertiary level care hospital for further management by reconstructive surgeons.

IV. RESULTS

Characteristics	Parameter	Total
Gender	Male	29
Gender	Female	19
A ()	Mean	57.97
Age (years)	SD	15.3
ВМІ	Mean	28.89
DIVII	SD	7.5

Table 1- Demographic characteristics

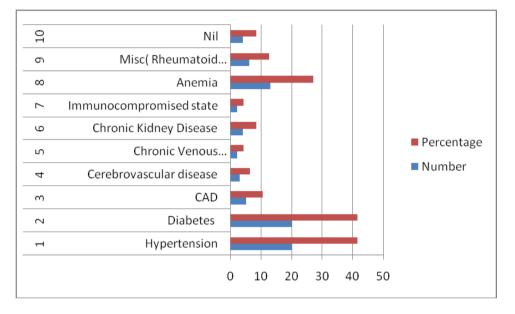
A total of 48 patients were registered for the study. 60% were males and 40% females. Most of them belonged to rural area with middle and lower middle class background, moderately working and consuming mixed diet. Age of patients ranged from 40 to 80 years with a mean of 57.97. **Co-morbidities**

	Table 2- Distribution of	Co-morbialities	
Serial No	Co-morbidity	Number	Percentage
1	Hypertension	20	41.66
2	Diabetes	20	41.66
3	CAD	5	10.41
4	Cerebro-vascular disease	3	6.25

Table 2- Distribution of Co-morbidities	5
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5	Chronic Venous Insufficiency/DVT	2	4.16
6	Chronic Kidney Disease	4	8.33
7	Immune-compromised state	2	4.16
8	Anemia	13	27.08
9	Misc (Rheumatoid arthritis/Osteoarthrosis)	6	12.5
10	Nil	4	8.33

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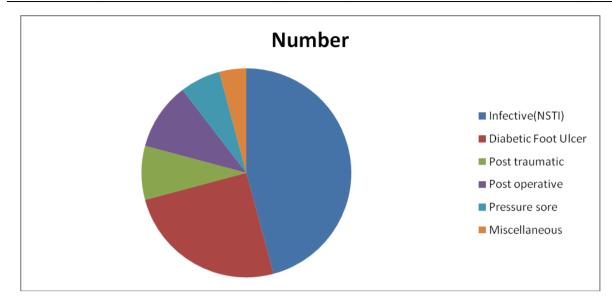


91.6 % (44 out of 48) had one or more co morbidities as listed in Table 2. They were on irregular treatment for the same. Drug compliance was very poor among the study group in view of ignorance, busy working schedule (daily wage labourers), distantly situated medical facility and lack of awareness. Hypertension and Type II Diabetes mellitus were among the most common associated co-morbidities. Diabetes mellitus, Cardiac disease and CVA were found to be associated with the NSTI cases in addition to the diabetic foot/ulcer patients. Anaemia was noted in 27.08 % cases. However, it is felt that it was more likely due to the disease process (sepsis) rather than cause of it (based upon the inputs received while taking history). Chronic Kidney disease, chronic venous insufficiency and Immune-compromised states (HIV +ve) constituted 2-3 cases each. It was found that trivial trauma, scratching, furunculosis and infection in previously healed ulcer were triggering factors for infection and creation of large soft tissue loss. Out of the 4 patients without any co-morbidity, three were NSTI cases and one post-traumatic wound.

Wound Type and Their Distribution

Table	3	- Types	of	Wound
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Etiology	Number	Percentage
Infective(NSTI)	22	45.83
Diabetic Foot Ulcer	12	25.0
Post traumatic	4	8.33
Post operative	5	10.41
Pressure sore	3	6.25
Miscellaneous	2	4.25



As seen from the table No 3, necrotizing soft tissue infection (NSTI) was the most common cause of extensive skin and soft tissue loss and creation of large wounds followed by diabetic ulcers. However in cases of diabetic ulcers, post operative wounds too, a component of infection was witnessed. NSTI as a primary presentation or developing secondarily in a diabetic ulcer resulted in large areas of skin and soft tissue loss which required debridement for removing dead and deadly tissue. These wounds required initial 2-3 debridement under anaesthesia to get a healthy tissue bed, control of infection and removal of infected tissue. Once a healthy bed has been achieved, NPWT was deployed to get complete granulation tissue. Diabetic ulcers had associated skin loss including deep seated abscess tracts along the tendon sheaths of foot and ankle thereby affecting underlying muscles and bones with or without osteomylitic. Such wounds needed thorough debridement, at times required amputation of the extremity to remove osteomylitic bone. Over a period, once the healthy tissue appeared with no signs of active infection, these wounds were selected for NPWT.

Road traffic accidents with high impact trauma resulted in large exposed areas of tissue loss in posttraumatic cases. Though, these wounds were not primarily infected but had great potential to develop the same. Aggressive debridement, removal of dirt, debris and de-vascularised tissue and early NPWT showed good response. Pressure sores were seen in patients who were bed-ridden with multiple medical co-morbidities. In view of multiple associated co morbidities, large area at gravity dependent areas, management was indeed challenging. Half of such cases required management at specialised plastic surgery centres and were referred accordingly.

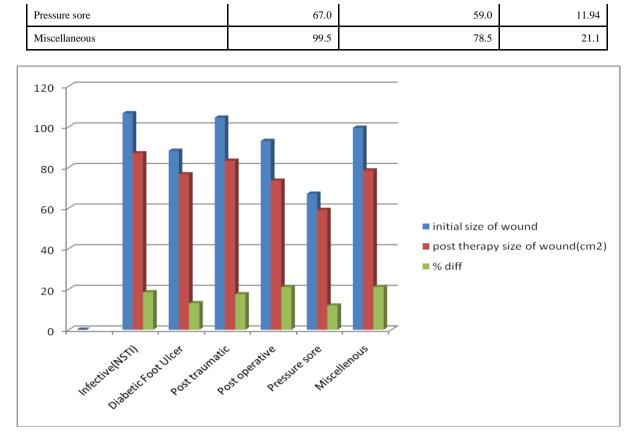
Post-operative wounds were due to surgical site infection which in turn could be attributed to patientrelated risk factors and procedure-related risk factors. [7] Old age, pre-existing hypovolemia due to sepsis, malnutrition, obesity, patients on long-standing steroids, overt / uncontrolled diabetes, patients on immunosuppressive drugs, smoking and presence of coexistent infection at a remote site are some of the risk factors of the former. Procedure-related risk factors include formation of a hematoma at the operation site, use of a foreign material like drain, leaving dead space during wound closure, previous infection at the site of incision, duration of surgical scrub, preoperative shaving, poor skin preparation, long surgery, poor surgical technique, hypothermia, contamination from the operating room, and prolonged peri-operative stay in hospital.

Miscellaneous cases included one deep tubercular abscess in perineum and one tubercular abscess of breast with large surface area of skin and breast tissue loss. Both the cases are confirmed tuberculosis by histopathology and hence kept as a separate entity.

Type of Wound	Initial size of wound (cm2)	Post therapy size of wound(cm2)	% diff
Infective(NSTI)	106.65	86.95	18.47
Diabetic Foot Ulcer	88.15	76.58	13.12
Post traumatic	104.5	83.25	17.52
Post operative	93.0	73.4	21.07

Effect of NPWT on size of wound

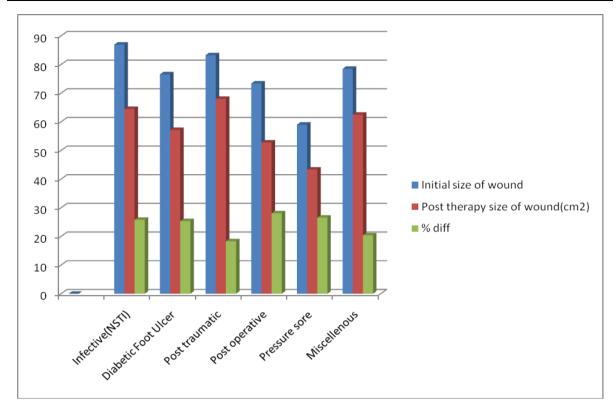
Table 4- Wound size after first NPWT session



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Table 5- Wound size after second NPWT session

Type of Wound	Initial size of wound (cm2)	Post therapy size of wound(cm2)	% diff
Infective(NSTI)	86.95	64.5	25.81
Diabetic Foot Ulcer	76.58	57.16	25.35
Post traumatic	83.25	68.0	18.31
Post operative	73.4	52.8	28.06
Pressure sore	59.0	43.33	26.55
Miscellenous	78.5	62.5	20.38



In our study, there was significant reduction in the size of wound after application of NPWT in NSTI wounds, diabetic and post-traumatic ulcers. Post-operative wounds showed reduction in wound size by more than 50%. The neuropathic and trophic ulcers like pressure sores showed less than 20% reduction in wound size. Second sitting of NPWT showed better results in terms of reduction in size of the wounds as compared with the first sitting. On an average 30 % reduction in size of the wound was found in almost all wounds. It was also observed that prolonging the duration of NPWT in one session did not show much advantage and five days session was quite adequate for the study.

Large wounds due to pressure sores (Grade IV) over ischial and gluteal regions were treated with two sessions of NPWT. However, in view of their large size, uneven surface in difficult areas and associated medical co-morbidities, these patients were referred to tertiary care centres for further management by Plastic / Reconstructive Surgeon.

	After 1 St session of NPWT- Dept	h	
Type of wound	Initial depth of wound (mm)	Post therapy depth of wound (mm)	% Diff
Infective(NSTI)	29.18	23.4	19.8
Diabetic Foot Ulcer	22.25	18.58	16.49
Post traumatic	25.75	20.25	21.35
Post operative	24.2	18.2	24.7
Pressure sore	10.33	8.66	16.16
Miscellaneous	29.0	24.5	15.51

Table 5 - Wound depth after 1st session of NPWT

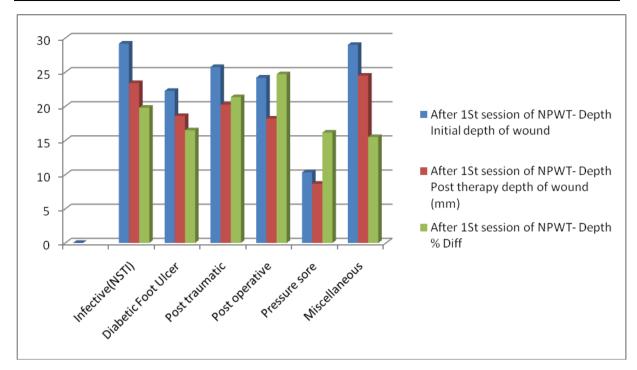
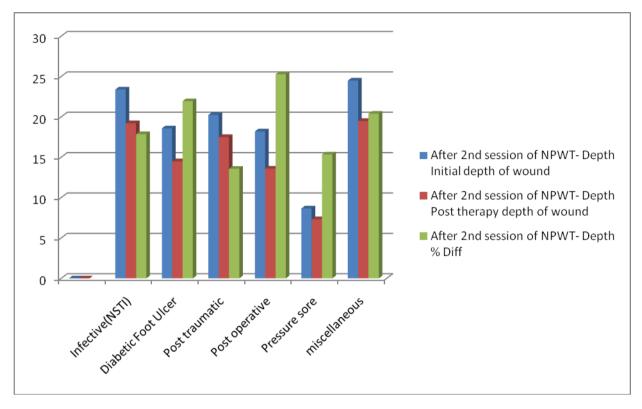


Table 6- Wound depth after seco	ond session of NPWT
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Wound depth after 2 nd session of NPWT- Depth						
Type of Wound	Initial depth of wound (mm)	Post therapy depth of wound (mm)	n of wound % Diff			
Infective(NSTI)	23.4	19.22	17.86			
Diabetic Foot Ulcer	18.58	14.5	21.95			
Post traumatic	20.25	17.5	13.58			
Post operative	18.2	13.6	25.27			
Pressure sore	8.66	7.33	15.35			
miscellaneous	24.5	19.5	20.4			



The depth of wounds in our study was ranging from 9 to 43 mm. Pressure sores were the deepest amongst all. Reduction in depth of wound was significant ranging from 20 - 40 % in both sessions. Second session of NPWT proved to be more effective in reducing size of wound rather than depth of wound which could be because of presence of foam material. Post-operative wounds showed relatively better results from NPWT.

Figure no 1



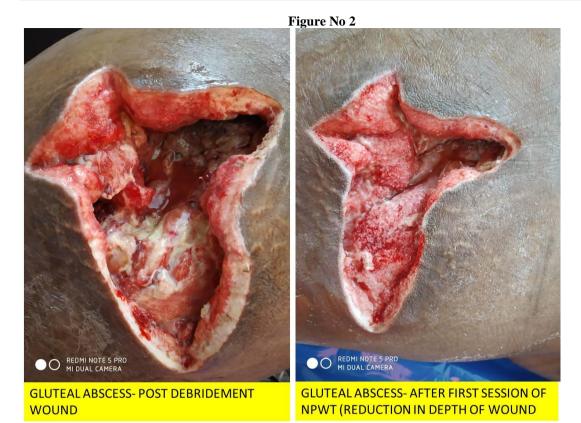


Figure no 3



GLUTEAL ABSCESS (OPTD)- AFTER SECOND SESSION OF NPWT

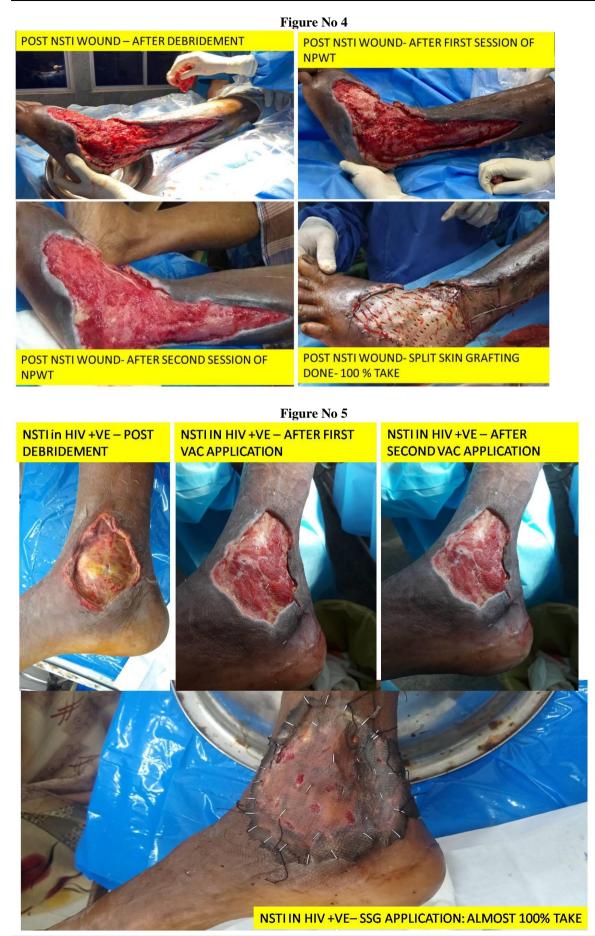


GLUTEAL ABSCESS (OPTD)- AFTER FIRST SESSION OF NPWT



GLUTEAL ABSCESS (OPTD)- AFTER SECONDARY SUTURING

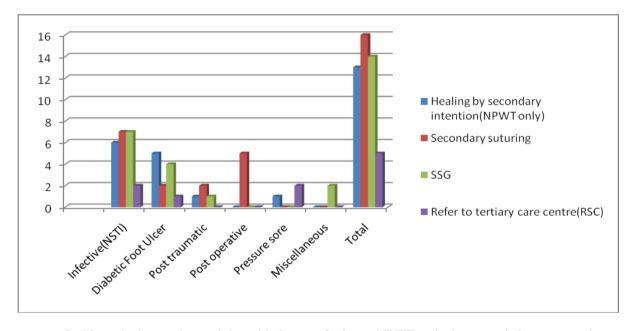




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Table 6: Definitive closure modality							
Type of wound	Healing by secondary intention (NPWT only)	Secondary suturing	SSG	Refer to Tertiary care centre(RSC)			
Infective(NSTI)	6	7	7	2			
Diabetic Foot Ulcer	5	2	4	1			
Post traumatic	1	2	1	0			
Post operative	0	5	0	0			
Pressure sore	1	0	0	2			
Miscellaneous	0	0	2	0			
Total	13	16	14	5			

Definitive closure of all the wounds



In this study, it was observed that with the use of primary NPWT and other wound closure strategies as a supplementary procedure, definitive skin cover was successfully achieved in almost all the wounds. We were able to close all the post-operative wounds by secondary suturing after one or two sessions of NPWT. Infected wounds mostly secondary to the necrotising soft tissue infection (NSTI) and loss of subcutaneous and skin cover required extensive debridement to start with and two sessions of NPWT and were later managed with split skin grafting. Almost 25 % of the wounds were successfully treated by using NPWT only and did not require any other surgical intervention for achieving skin cover. Two cases of NSTI and one each of a large pressure sore and diabetic ulcer had to be referred to higher centre for management by reconstructive surgeon for flap cover.

V. DISCUSSION

Surgical wound management is the most important aspect of surgical procedure as it is related with the sense of complete recovery for the patient. An open wound is considered to have high probability to get infected again. NPWT is one of the most studied subjects with respect to wound healing worldwide. Our study is an observational study in a secondary care zonal hospital providing speciality health care services to mostly semi urban and rural population. The study is focused on analysis of demographic parameters, types of wounds encountered in the dependent clientele population, prevalence of the co morbidities and their effect on recovery of the wound while using the NPWT and requirement of other surgical procedures to achieve complete viable skin cover over the wound. [8] [9]

The positive effect of NPWT in achieving faster rate of healing has been dwelled upon since last two decades and has been validated by numerous studies. [10] [11] [12] [13] [14]. Vuerstaek et all [15] demonstrated its efficacy in wound bed preparation. In our study also we could achieve significant decrease in depth of the

wound. However, in our study average size as well as depth of wounds was much higher and hence the results need to be analysed accordingly.

Chronic wounds with large area of skin and subcutaneous tissue loss is mostly seen in 4th decade onwards due to addition of multiple co morbidities at that particular age. Instead, young population is more likely to present with post operative or post traumatic skin and soft tissue loss forming large wound surface requiring NPWT. Diabetes Mellitus and hypertension cause microangiopathy and arteriosclerosis, which slows down the wound healing process. Skin and soft tissue infections are common in diabetics. Moreover these conditions also cause flaring up of small wounds resulting from disruption of the skin barrier, trauma, pressure, or local ischemia to extensive necrotising soft tissue infection creating a larger wound surface with deeper tissue involvement along the fascial and tendino-muscular planes. This is due to secondary infection or development of adjacent soft tissue or deeper bone infection. [16]

In our study similar statistics are seen as mean age of our study population is 57.4 with diabetes mellitus and hypertension as more commonly associated co morbidities in almost 85 % of cases. Gender does not seem to play a major role as distribution is almost equal. Though males seem to be more commonly presenting with larger wound surface as compared to females, it is most likely due to their outdoor working in farms / fields as compared to females. Younger patients presented with large wound surface are mostly post-traumatic in nature due to road traffic accidents. As far as the result of NPWT in younger patients in our study, it did not show any significant difference in speed of wound healing as compared with the older population with wounds from other aetiologies.

Complicated diabetic foot which includes variety of soft tissue loss from skin to affection of muscles and bone necrosis were encountered and formed a large group in the study which required NPWT. All such cases were subjected to thorough surgical wound debridement to remove dead, necrotic and infected material. In addition to altering the environment of the chronic wound, surgical debridement is aimed at removing nonviable and necrotic tissue which is detrimental to healing. Hyper-keratotic epidermis (callus) and necrotic dermal tissue, foreign debris, and bacterial elements are known to form abnormal wound bed and wound edge tissue which has an inhibitory effect on wound healing. [17] Theoretically, hypertension can increase the thrombosis and arteriosclerosis of arteries supplying the skin, predisposing the area to a necrotising infection. Diabetes mellitus is associated with immune deficiencies and arteriosclerosis, both increasing the risk of developing infection. [18]

Blume et all [19] found additional advantage of NPWT over Advance Moist Wound Therapy (AMWT) alone (predominantly alginates, hydrogels) and found 43.2% of complete wound healing with use of only NPWT as compared to 28.9% in the AMWT group. The healing rate was significantly faster in NPWT group. In a randomised controlled study by David G Armstrong et al [20] on role of NPWT post partial amputation, found average wound size of 20.7cm2 and 56% of patients having complete healing of wound with NPWT alone. Similar results with regard to faster healing, reduction in wound size and overall improvement of wound condition aiding in complete healing have been validated by evidence based review studies. [21] [22] In our study the average size of the wound is almost 4 times bigger and not all of them were post amputee wounds, still the results are quite comparable showing reduction in size and depth by 25-28 %.

AyhanKilic et al [23] studied effect of NPWT in surgical site infections and found that NPWT resulted in clinical and bacteriologic eradication of infections in 64.7% of cases and significant reduction in wound size. Our study also achieved nearly 55% of reduction in wound size post 02 sessions of NPWT. Management of large wounds in anatomically difficult areas always poses a challenge. Even application of NPWT in such region is technically challenging with high chances of leakage in seal, frequent soiling of the dressing. In certain cases it requires even addition of the stool diversion procedures prior to application of NPWT. Silberstein et all [24] found NPWT to be useful in large wound management in difficult anatomical location in case of Fournier's gangrene.

Misiakos et al [25] incorporated use of NPWT as one of the best modalities in management of Necrotising soft tissue infections in their review article. While most of these studies involved wound sizes of 40 to 50 cm2, the results in our study with fairly larger size of wounds (Average size 100cm2 and avg depth 25mm) have been found comparable and better in a few, in terms of number of sessions of NPWT required prior to definitive closure. Early debridement of wound for removal of infected tissues and opening up the inter-tissue planes for achieving relatively better surface proved to be beneficial. NPWT was applied after 24-48 hrs once adequate haemostasis was achieved. Adequate seal, moderate suction and un-interrupted negative pressure by using NPWT were proved to be beneficial for definitive wound closure in our study. Whilst the patients in our study were from rural background, adequate counselling and patient cooperation for maintaining uninterrupted seal was of paramount importance.

In addition to this , we also found NPWT has an added advantage of providing a longer temporary wound cover to the wound after initial debridement, reduced the pain due to daily dressing and chemical / mechanical wound debridement. As seen from the demographic distribution, and associated co morbidities,

repeated surgical debridement, trauma of dressing and release of cytokines causing difficulty in recovery from sepsis were avoided by providing a prolonged but effective wound cover. NPWT gives an added advantage of faster healing too.

Chun-yu-Chen et al [26] used NPWT extensively post debridement in sacral pressure ulcers with large initial defect and subsequently used V–Y advancement flaps for closure. In our case the results of pressure sore in sacral area were not as encouraging. Though we could achieve healthy granulation tissue cover in two cases still definitive closure required reconstructive surgery management. Cushing et al [27] in their extensive evidence based publication on management of pressure sores mentioned management of eight cases of pressure sores mostly of sacral region were managed with NPWT.

Negative pressure wound therapy compared with standard dressing in the post-operative wounds may reduce the chances of SSI however it may be applicable in small sized wounds. Larger sized wounds as in our study had higher chances of secondary infection. Use of NPWT in primary closure of surgical wounds was studied in the Cochrane review by Webster et. al. [28] However in our study NPWT had shown very good results in closure of post-operative wounds with SSI. All the wounds could be closed with secondary suturing and did not require other special techniques like STSG or flap cover. The results in cases of post-operative wounds with SSI, when managed with NPWT and secondary suturing were akin to the primary closure.

In our study the depth of wound has shown significant reduction after the first session as compared to the second session which is opposite to the results as observed in terms of reduction in size of the wound. In one of the experimental study involving animal model and live animal muscles, it was observed that effect of negative pressure was transferred to interstitial fluid for not more than 2 mm from the foam surface. The study used the pressure mode of -50.-75 and -125 mm HG settings to demonstrate the same. [29] Hence it is likely to be related more to the depth of pressure rather than the presence of foam material. Hence it can be concluded that NPWT provides environment to drain the interstitial fluid, promotes formation of granulation tissue which works more in contracting the size of the wound more than reducing depth of wound.

VI. CONCLUSION

At present, NPWT has been accepted worldwide as standard of care in management of complex wounds. In this study we have observed the known effects of NPWT at our secondary care hospital and shared our experience. This study concludes that the effect of NPWT is gender neutral. Presence of co morbidities may have an adverse effect over results of the therapy however the same is not covered in the scope of this study. NPWT has surely been beneficial in reduction in the size and depth of wound however reduction in size is more significant than that of reduction in depth of wound. Especially wounds arising from infection like NSTI and complicated diabetic foot have shown better results as compared with the pressure sores. Despite the application of NPWT, larger wounds require assistance of other surgical procedures to achieve adequate and viable skin cover. Results in this study are comparable with existing data and shows important role of NPWT in cases of large wounds arising from various causes in reducing morbidity in patients.

REFERENCES

- [1]. Miller C. The History of Negative Pressure Wound Therapy (NPWT): From "Lip Service" to the Modern Vacuum System. J Am Coll Clin Wound Spec. 2013 Nov 28;4(3):61-2. doi: 10.1016/j.jccw.2013.11.002. PMID: 26236637; PMCID: PMC4511545.
- [2]. Morykwas MJ, Simpson J, Punger K, Argenta A, Kremers L, Argenta J. Vacuum-assisted closure: state of basic research and physiologic foundation. Plast Reconstr Surg. 2006 Jun;117(7 Suppl):121S-126S. doi: 10.1097/01.prs.0000225450.12593.12. PMID: 16799379.
- [3]. Lalezari S, Lee CJ, Borovikova AA, Banyard DA, Paydar KZ, Wirth GA, Widgerow AD. Deconstructing negative pressure wound therapy. Int Wound J. 2017 Aug;14(4):649-657. doi: 10.1111/iwj.12658. Epub 2016 Sep 29. PMID: 27681204; PMCID: PMC7949947.
- [4]. ActiV.A.C.® Therapy System Kinetic Concepts PDF Catalogs | Technical Documentation (medicalexpo.com)
- [5]. (Negative Pressure Wound Therapy Technology (mykci.com) last viewed on 30 Nov 2022).
- [6]. Harris C, Bates-Jensen B, Parslow N, Raizman R, Singh M, Ketchen R. Bates-Jensen wound assessment tool: pictorial guide validation project. J Wound Ostomy Continence Nurs. 2010 May-Jun;37(3):253-9. doi: 10.1097/WON.0b013e3181d73aab. PMID: 20386331.
- [7]. Zabaglo M, Sharman T. Postoperative Wound Infection. 2022 Sep 19. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2022 Jan–. PMID: 32809368.
- [8]. Witkowski W, Jawien A, Witkiewicz W, Zon B. Initial multi-centre observations upon the effect of a new Topical Negative Pressure device upon patient and clinician experience and the treatment of wounds. Int Wound J. 2009 Apr;6(2):167-74. doi: 10.1111/j.1742-481X.2009.00586.x. PMID: 19432667; PMCID: PMC7951371.
- [9]. Pertea, M.; Poroch, V.; Ciobanu, P.; Filip, A.; Velenciuc, N.; Lunca, S.; Panuta, A.; Buna-Arvinte, M.; Luca, S.; Veliceasa, B. Efficiency of Bromelain-Enriched Enzyme Mixture (NexoBridTM) in the Treatment of Burn Wounds. Appl. Sci. 2021, 11, 8134. https://doi.org/10.3390/ app11178134
- [10]. Armstrong DG, Lavery LA; Diabetic Foot Study Consortium. Negative pressure wound therapy after partial diabetic foot amputation: a multicentre, randomised controlled trial. Lancet. 2005 Nov 12;366(9498):1704-10. doi: 10.1016/S0140-6736(05)67695-7. PMID: 16291063.
- [11]. Kiliç A, Ozkaya U, Sökücü S, Basilgan S, Kabukçuoğlu Y. Cerrahi alanda gelişen enfeksiyonların tedavisinde vakum yardimli örtüm sistemi uygulamalarimiz [Use of vacuum-assisted closure in the topical treatment of surgical site infections]. Acta Orthop Traumatol Turc. 2009 Aug-Oct;43(4):336-42. Turkish. doi: 10.3944/AOTT.2009.336. PMID: 19809231.

- [12]. Stansby G, Wealleans V, Wilson L, Morrow D, Gooday C, Dhatariya K. Clinical experience of a new NPWT system in diabetic foot ulcers and post-amputation wounds. J Wound Care. 2010 Nov;19(11):496, 498-502. doi: 10.12968/jowc.2010.19.11.79706. PMID: 21135798.
- [13]. Nain PS, Uppal SK, Garg R, Bajaj K, Garg S. Role of negative pressure wound therapy in healing of diabetic foot ulcers. J Surg Tech Case Rep. 2011 Jan;3(1):17-22. doi: 10.4103/2006-8808.78466. PMID: 22022649; PMCID: PMC3192517.
- [14]. Blume PA, Walters J, Payne W, Ayala J, Lantis J. Comparison of negative pressure wound therapy using vacuum-assisted closure with advanced moist wound therapy in the treatment of diabetic foot ulcers: a multicenter randomized controlled trial. Diabetes Care. 2008 Apr;31(4):631-6. doi: 10.2337/dc07-2196. Epub 2007 Dec 27. PMID: 18162494.
- [15]. Vuerstaek JD, Vainas T, Wuite J, Nelemans P, Neumann MH, Veraart JC. State-of-the-art treatment of chronic leg ulcers: A randomized controlled trial comparing vacuum-assisted closure (V.A.C.) with modern wound dressings. J Vasc Surg. 2006 Nov;44(5):1029-37; discussion 1038. doi: 10.1016/j.jvs.2006.07.030. Epub 2006 Sep 26. PMID: 17000077.
- [16]. Polk C, Sampson MM, Roshdy D, Davidson LE. Skin and Soft Tissue Infections in Patients with Diabetes Mellitus. Infect Dis Clin North Am. 2021 Mar;35(1):183-197. doi: 10.1016/j.idc.2020.10.007. Epub 2020 Dec 7. PMID: 33303332.
- [17]. Lebrun E, Tomic-Canic M, Kirsner RS. The role of surgical debridement in healing of diabetic foot ulcers. Wound Repair Regen. 2010 Sep-Oct;18(5):433-8. doi: 10.1111/j.1524-475X.2010.00619.x. PMID: 20840517.
- [18]. Anca M. Avram; Case Study: Necrotizing Fasciitis in a Patient With Obesity and Poorly Controlled Type 2 Diabetes. Clin Diabetes 1 October 2002; 20 (4): 198–200. https://doi.org/10.2337/diaclin.20.4.198
- [19]. Blume PA, Walters J, Payne W, Ayala J, Lantis J. Comparison of negative pressure wound therapy using vacuum-assisted closure with advanced moist wound therapy in the treatment of diabetic foot ulcers: a multicenter randomized controlled trial. Diabetes Care. 2008 Apr;31(4):631-6. doi: 10.2337/dc07-2196. Epub 2007 Dec 27. PMID: 18162494.
- [20]. Armstrong DG, Lavery LA; Diabetic Foot Study Consortium. Negative pressure wound therapy after partial diabetic foot amputation: a multicentre, randomised controlled trial. Lancet. 2005 Nov 12;366(9498):1704-10. doi: 10.1016/S0140-6736(05)67695-7. PMID: 16291063.
- [21]. Guffanti A. Negative pressure wound therapy in the treatment of diabetic foot ulcers: a systematic review of the literature. J Wound Ostomy Continence Nurs. 2014 May-Jun;41(3):233-7. doi: 10.1097/WON.0000000000021. PMID: 24805174.
- [22]. Vig S, Dowsett C, Berg L, Caravaggi C, Rome P, Birke-Sorensen H, Bruhin A, Chariker M, Depoorter M, Dunn R, Duteille F, Ferreira F, Martínez JM, Grudzien G, Hudson D, Ichioka S, Ingemansson R, Jeffery S, Krug E, Lee C, Malmsjo M, Runkel N; International Expert Panel on Negative Pressure Wound Therapy [NPWT-EP]: Martin R, Smith J. Evidence-based recommendations for the use of negative pressure wound therapy in chronic wounds: steps towards an international consensus. J Tissue Viability. 2011 Dec;20 Suppl 1:S1-18. doi: 10.1016/j.jtv.2011.07.002. Epub 2011 Nov 25. PMID: 22119531.
- [23]. Kiliç A, Ozkaya U, Sökücü S, Basilgan S, Kabukçuoğlu Y. Cerrahi alanda gelişen enfeksiyonların tedavisinde vakum yardimli örtüm sistemi uygulamalarimiz [Use of vacuum-assisted closure in the topical treatment of surgical site infections]. Acta Orthop Traumatol Turc. 2009 Aug-Oct;43(4):336-42. Turkish. doi: 10.3944/AOTT.2009.336. PMID: 19809231.
- [24]. Silberstein J, Grabowski J, Parsons JK. Use of a Vacuum-Assisted Device for Fournier's Gangrene: A New Paradigm. Rev Urol. 2008 Winter;10(1):76-80. PMID: 18470279; PMCID: PMC2312348.
- [25]. Misiakos EP, Bagias G, Patapis P, Sotiropoulos D, Kanavidis P, Machairas A. Current concepts in the management of necrotizing fasciitis. Front Surg. 2014 Sep 29;1:36. doi: 10.3389/fsurg.2014.00036. PMID: 25593960; PMCID: PMC4286984.
- [26]. Chen, Chun-Yu MDa,b; Chiang, I-Han MDa; Ou, Kuang-Ling MD, PhDa; Chiu, Yu-Lung PhDc,d; Liu, Hung-Hui MDa; Chang, Chun-Kai MDa; Wu, Chien-Ju MDa; Chu, Tzi-Shiang MDa; Hsu, Kuo-Feng MDa; Huang, Dun-Wei MDa; Tzeng, Yuan-Sheng MDa,*. Surgical treatment and strategy in patients with pressure sores: A single-surgeon experience. Medicine 99(44):p e23022, October 30, 2020. | DOI: 10.1097/MD.00000000023022
- [27]. Cushing CA, Phillips LG. Evidence-based medicine: pressure sores. Plast Reconstr Surg. 2013 Dec;132(6):1720-1732. doi: 10.1097/PRS.0b013e3182a808ba. PMID: 24281597.
- [28]. Webster J, Liu Z, Norman G, Dumville JC, Chiverton L, Scuffham P, Stankiewicz M, Chaboyer WP. Negative pressure wound therapy for surgical wounds healing by primary closure. Cochrane Database Syst Rev. 2019 Mar 26;3(3):CD009261. doi: 10.1002/14651858.CD009261.pub4. Update in: Cochrane Database Syst Rev. 2020 May 1;5:CD009261. PMID: 30912582; PMCID: PMC6434581.
- [29]. Murphey GC, Macias BR, Hargens AR. Depth of penetration of negative pressure wound therapy into underlying tissues. Wound Repair Regen. 2009 Jan-Feb;17(1):113-7. doi: 10.1111/j.1524-475X.2008.00448.x. PMID: 19152658.