REVIEW

Evaluating the Efficacy of Aggressive Treatments and Palliative Care for Traumatic Brain Injuries in Elderly Patients: A Review

Mukti H. Patel, BSc Student [1]*, Nidhi D. Mehta, BSc Student [1]

[1] Department of Schulich Medicine and Dentistry, University of Western Ontario, London, Ontario, Canada N6A 3K7

*Corresponding Author: mpate422@uwo.ca

Abstract

Introduction: Traumatic brain injuries (TBIs) are caused by trauma to the head or body, and are a prominent issue within the geriatric population. Severe TBIs can result in a myriad of symptoms including headaches, problems with speech, loss of consciousness, coma, and potential death.

Methods: The goal of this paper is to determine if aggressive treatment would be better suited to treat severe TBIs in the elderly population as compared to the standard cons. A primary literature search was conducted using PubMed, EMBASE, and Google Scholar, and 9 articles were chosen based on the inclusion and exclusion criteria identified.

Results: It was found that aggressive treatments such as depressive craniotomies are effective in treating TBIs, improving GCS scores and decreasing mortality rates. Despite this, aggressive treatment cannot be universally applied, as many factors beyond age contribute to the type of treatment that can be administered. Furthermore, when aggressive treatment could not be used, palliative care is useful in treating TBIs in the elderly population, but it does not contribute significantly to the decrease in mortality.

Discussion: As a result, the study concludes that while aggressive treatment is often more beneficial than palliative care, the specific combinatorial of these treatments should be considered based on the individual needs and medical history of each patient

Conclusion: This finding is essential as it contributes to the limited body of knowledge currently available for the treatment of TBIs in the elderly population.

Keywords: traumatic brain injury; palliative care; craniotomies

Introduction

Traumatic brain injuries (TBIs) result from head trauma and stand as one of the leading causes of disability and mortality worldwide. Falls, motor vehicle crashes, firearm-related incidents, and assaults are among the most common causes of TBIs. The injuries can be broadly categorized into penetrating TBIs, caused by objects piercing the skull and entering the brain tissue, and nonpenetrating TBIs, resulting from forceful impacts that cause the brain to move within the skull. The severity of a TBI can vary depending on the type and extent of the trauma caused. Mild TBIs result in less severe symptoms including headaches, nausea, fatigue, problems with speech, loss of balance, as well as a myriad of sensory issues such as blurred vision and sensitivity to light [1]. In the case of mild TBIs, most patients generally recover in a week up to three months. Contrastingly, it can take patients a few weeks up to a few years to fully recover from severe TBIs. For moderate to severe TBIs, in addition to the symptoms listed above, patients can suffer convulsions, seizures, clear fluids draining from the nose or ears, loss of consciousness,

Patel et al. | URNCST Journal (2023): Volume 7, Issue 10 DOI Link: <u>https://doi.org/10.26685/urncst.527</u> confusion, mood changes, and others. Untreated TBIs can lead to the perpetuation of the symptoms listed above, and in the most severe cases, patients can fall into a vegetative state, coma, and in the worst scenarios, brain death. [1].

TBIs are most prevalent in young children, young male adults, and individuals over the age of 55. Despite an extensive body of research exploring TBI epidemiology, symptoms, and treatment in young male adults, fewer studies have investigated the treatment of older TBI patients. However, elderly patients with severe TBI have a poorer prognosis than younger patients, including higher mortality rates. This is due to the higher probability of having pre-existing systemic diseases such as arthritis or the use of antithrombotic medications such as warfarin that impair treatment measures [1]. With the increasing aging population, there is an urgent need to develop guidelines or protocols for treatment decisions in elderly patients with moderate to severe TBIs.

Treatment methods for severe TBIs can be broadly categorized into aggressive surgical treatment and conservative (non-surgical) treatment. Aggressive surgical



treatment involves invasive surgical procedures, such as craniotomies, endoscopic ventriculostomies, or ventriculoperitoneal shunt surgery. In contrast, the conservative treatment/palliative care (PC) performs all the standard practices of non-surgical medical treatment. PC includes monitoring of the illness, pain management, and emotional support. The articles screened varied in the PC provided, but upheld the primary pillars: symptom management, emotional support and spiritual care. PC also encourages various family discussions, allowing the patient to be able to discuss the different treatments. With such a high mortality rate in the elderly populations, physicians might opt for non-surgical intervention and reduce treatment intensity. However, this could be a self-fulfilling prophecy: patients could be undertreated which resulted in higher mortality in elderly patients with severe TBI. For instance, a study conducted by Wan et al. suggested that surgical intervention led to better clinical outcomes compared to conservative (non-surgical) treatment in elderly patients [2]. Other studies have reported worse outcomes [3]. To further complicate treatment decisions in elderly patients, older patients have a 1-year mortality of 50% after hospital discharge. Long-term disability is also prevalent in this group. Functional dependency and the need for significant rehabilitation is burdensome for both patients and caregivers. Older patients might value quality of life over quantity, and they might opt for PC rather than life-prolonging treatment. Despite patients' preferences, PC might not be integrated or administered in a timely manner for fear of undertreating the patients. As a result of these uncertainties and controversies, there is a high practice variation in the management of elderly patients with severe TBI.

This review article aims to synthesize current studies to determine the optimal intervention in the elderly population with severe TBI. In this work, the treatment outcomes of aggressive (surgical) and conservative (non-surgical medical) interventions were compared, and the impact of PC on the quality of care in older TBI patients was assessed.

Methods

Preliminary searches were conducted using PubMed, EMBASE, and Google Scholar. Important topics related to TBI and the elderly were first identified through initial research to determine the state of the literature and identify areas with knowledge gaps, while looking into the current treatment for TBIs. 48 articles were collected through this initial search. Based on these articles, it was determined that the topic of interest should be on surgical treatments versus conservative approaches with or without PC consultation for elderly patients with TBIs. Searches were restricted to articles that were published in 2013 or later. The keywords "elderly patients and TBI", "craniotomy procedure for elderly TBI patients", "conservative treatment vs aggressive treatment", "TBI elderly patients and bias" and "palliative care/ end-of-life care for TBI elderly patients", were applied to the databases listed above. Articles were selected according to the following inclusion criteria:

- (1) Title/ abstract and main text must include an intervention related to the research question. Neurosurgical procedures including craniotomy surgery, endoscopic ventriculostomy, decompressive craniectomy, and cranioplasty were classified as an 'aggressive treatment', while medical treatments with palliative care were classified as 'PC'. PC is defined as the interdisciplinary approach that minimizes invasive procedures and improves quality of life of patients and their families.
- (2) Recruited patients in the study that are listed as the "elderly" patients must be older than 55 years old,
- (3) GCS score to determine severity of TBI would be between 3 to 8 so as to be classified as a 'severe' TBI
- (4) Methods must include a specific intervention with specific outcomes related to the research question – the study should report the mortality rate or functional outcome as a result of the selected intervention
- (5) Study should have adequate patients for assessment, i.e., > total of 50 patients from all of the groups in each study. Studies that focused on case studies in which only a small subset of patients with TBIs were excluded.

From the 48 initial articles, 9 retrospective studies were selected. 1 assessed the treatment intensity with age, 4 examined the treatment outcomes of aggressive treatment (i.e., craniotomies) versus conservative treatment, and 4 investigated the impact of PC in elderly patients.

Results

<u>Table 1</u> provided a summary of all the studies. Intensity of management of patients with TBI decreased with age irrespective of head injury severity [4]. Importantly, increasing age and low intensity management were associated with increased risk of 30-day mortality [4]. This confirmed the skepticism regarding physicians undertreating elderly TBI patients.

	Authors	Study populations	Type of treatments	Outcome	Major relevant findings
1	Skaansar et al., 2020	612 elderly TBI patients (≥ 65 years old) and 959 non-elderly patients (<65 years old)	Experimental: TBI Patients >65 years old vs Control: TBI Patients <65 years old	30 day mortality in the age groups 65–74 years, 75–84 years and \geq 85 years was 11%, 23% and 24%; while 30 day mortality rates for the age groups 15–54 years, and 55–64 years were 6% and 11%. Intensity of management of patients with TBI decreased with age; the low intensity management was associated with increased risk of mortality Trauma team activation, invasive ICP monitoring, TBI imaging, and ventilators treatment declined significantly as age increased (p < 0.001).	Lower management intensity for elderly patients could explain why mortality rates are higher for these age groups.
2	Wan et al., 2016	112 patients with traumatic intracranial hematoma: 70 patients underwent surgery and 42 patients underwent conservative (non-surgical medical) treatment	Experimental: Aggressive treatment (surgical removal of intracranial hematoma) vs Control: Conservative (non-surgical medical) treatment	Patients who underwent surgeries were less likely to have a low Glasgow Outcome Scale (GCS; 52% vs 95%) or mortality (33% vs 88%) 6 months after injury compared to patients treated conservatively.	Aggressive treatments may benefit those with higher Glasgow Outcome Scale scores.
3	Wutzler et al., 2015	4140 elderly TBI patients (≥ 60 years)	Experimental: Aggressive (surgical) treatment vs Control: Conservative (non-surgical medical) treatment	Conservative (non-surgical) treatment mortalities for patients in the age groups of 60-69, 70-79, and 80+ were 66.5 %, 68.9%, and 80.1%, respectively, while aggressive (surgical) treatment mortalities for the corresponding age groups were 43.9%, 39.6%, and 46.3%, respectively.	This study shows that neurosurgical procedures decrease mortality rates, and age alone should not be the reason for limited care and denial of surgeries.

Table 1. Article information, outcomes	, and major relevant findings for	or all 11 articles used in the article
----------------------------------------	-----------------------------------	----------------------------------------

	Authors	Study populations	Type of treatments	Outcome	Major relevant findings
4	Laic et al., 2023	149 patients (≥ 65 years) with sustained acute subdural hematoma: 32 patients underwent early surgery, 33 underwent delayed surgery, and 84 were conservatively treated.	Experimental: Aggressive treatment (a) early surgery (within 24h post- TBI), or (b) delayed surgery (> 24h post-TBI) vs Control: Conservative (non-surgical medical) treatment	56.4% patients were treated conservatively (non- surgical). 21.9% of early surgery patients, 3.0% of delayed surgery patients and 16.7% of non-surgical patients died within 30 days post-TBI, but this was not statistically significant ($p = 0.08$).	Although delayed surgery seems to provide better outcomes than early surgery, patients that underwent early surgery were presented with the most severe injuries at admission. With the limited sample size, future prospective larger-size study is required to draw conclusions.
5	Herou et al., 2015	119 elderly patients (≥ 70 years) who had sustained a closed TBI: 97 patients received surgeries, 22 patients received conservative (non- surgical) treatment.	Experimental: Aggressive (surgical) treatment vs Control: Conservative (non-surgical medical) treatment	30-day mortality in the surgically treated group was 36%, while the non-surgical group had a 30-day mortality of 23%.	Carefully selected elderly patients can benefit from surgery, but assessment should be done on a case by case basis.
6	Hwang et al., 2020	5733 TBI patients (\geq 55 years) with loss of consciousness \geq 24h: 2007 patients with palliative care (PC) and 3726 patients without	Experimental: Standard treatment with PC vs Control: Standard treatment without PC	PC utilization across the United States doubled in the past 5 years, but mortality rates remained the same. PC was used in 26% of surgically treated patients, and 35% nonsurgical patients. PC reduced the length of stay (3 days) compared to those without (12 days).	Current practice seems to take an all-or-nothing approach (i.e., surgery versus nonsurgical with PC). An integrative PC approach could facilitate timely administration and improve quality of care without sacrificing survival. PC reduces nonbeneficial life support and reduces length of hospital stay.

	Authors	Study populations	Type of treatments	Outcome	Major relevant findings
7	Lilley et al., 2016	90 patients (\geq 65 years) with severe TBI (initial GCS \leq 8): 32 patients with less severe TBI (GCS > 8 at 72 hours), 29 patients with severe TBI (GCS \leq 8), and 29 patients died within 3 days of admission.	Experimental: Patients with GCS ≤ 8 at 72 hours vs Control: Patients with GCS > 8 at 72 hours	Patients with GCS ≤ 8 at 72 hours had higher in-hospital (58.6% vs 6.2%) and 12- month (75.9% vs 40.6%) mortalities than patients with GCS > 8 at 72 hours. However, there is a lack of difference for functional dependency (100% vs 80%) between the two groups.	GCS scores at 72 hours predicted in-hospital death, but it is not a useful marker for long-term outcomes. Better prognostic markers are needed to provide guidelines to guide treatment decisions.
8	Wu et al., 2023	576 elderly patients (> 65 years) with TBI: 553 patients without palliative care (PC) versus 23 patients received PC. Among the 23 patients with PC, 14 received early PC and 9 received late PC.	Experimental: PC (a) early PC consultations (<8.6 days of admission), or (b) late PC consultations (>8.6 days of admission) vs Control: No PC (Standard treatment)	PC patients had longer hospital stays and higher costs, but these effects were minimized by early PC consultations. Early PC patients had significantly lower overall length of stay $(8.1 \pm 4.1 \text{ days vs } 22 \pm 16.6 \text{ day; p} = .0062)$ compared to late PC patients.	Although PC utilization is low, early PC consultation is correlated with shorter length of stay and reduced costs compared to late initiation of PC.
9	Lilley et al., 2018	34, 691 patients (median age = 79 years): 9983 patients at low mortality hospitals and 24,708 patients in all other hospitals.	Experimental: End-of-life care outcomes for patients at low- mortality hospitals vs Control: End-of-life care outcomes for patients at all other hospitals	Low-mortality hospitals had less in-hospital mortality (40% vs 53%), but higher 30-day mortality (16% vs 10%) than all other hospitals. However, cumulative 30-day mortality (55.8% vs 62.5%) was lower in low-mortality hospitals than other hospitals. Patients at low-mortality hospitals received fewer high-intensity end-of-life treatments and more hospice. Enrollment after discharge, while patients in other hospitals received more in-hospital palliative care (PC).	Low-mortality hospitals did not undertreat or discharge patients prematurely. However, low-mortality hospitals delivered PC without PC consultation (e.g., discussions about prognosis and goals of care). Although PC utilization do not compromise survival, further research on optimal delivery of PC is required.

Of the 4 articles that assessed treatment methods in the elderly, 3 studies reported favourable outcomes in patients treated with neurosurgical interventions compared to conservative (non-surgical) treatment. Wan et. al. showed that patients who underwent a craniotomy or depressive craniotomy were 42.3% and 55.2% less likely to have a low Glasgow Outcome Scale (GCS; score 1-3) and death, respectively [2]. Wultzer et. al. also demonstrated that postsurgical GCS score was higher for severe TBI patients who underwent aggressive surgical treatment as opposed to conservative treatment [5]. Interestingly, delayed surgery was reported to be more effective than early surgery, with a 3.0% mortality in late surgical patients compared to 21.0% in early surgical patients and 16.7% mortality in nonsurgical patients [6]. On the other hand, Herou et. al. showed that the 30-day mortality rate was higher (36% vs 23%) in neurosurgically treated patients compared to nonsurgical patients [3]. Further research on prognostic markers are needed to support treatment decisions in elderly patients.

In contrast, a study done by Lilley et al., displayed that the mortality rates did not increase in TBI elderly patients within the lower mortality hospitals, even though they performed less invasive surgical aggressive treatments [7]. However, a study done by Wu et al. stated that PC consultations helped reduce the length of stay in the hospital [8]. In this case, patients had a shorter length of stay (p=0.0062) and fewer ventilator days (p=0.030) as well as a higher quality of life after receiving treatment, in comparison to those that were not treated with PC [8]. This is similar to the findings of Hwang et al., where patients treated with PC had a significantly shorter length of stays than those without it (p<0.001) [9]. It was also found that PC was severely underutilized, despite its use leading to less intensity of care and a better quality of life after dischargement [9]. In a contradicting study, Skaansar et al., found that lower intensity management of TBI patients within the elderly did correlate with a higher risk of mortality [4]. Finally, an interesting finding was that the early administration of palliative consultation would reduce the length of hospital stay and cost to a greater degree than if administered later in the treatment process [8]. Thus, more research needs to be done within this area of TBI management with elderly patients.

Discussion

TBIs involve complex decision making, and it is even more challenging in the elderly populations with lots of uncertainties and controversies. Elderly patients with TBI are known to have a poor prognosis, but there is no evidence-based guideline for treatment decisions. Thus, age sometimes becomes a biased factor. While some physicians perform neurosurgical procedures (aggressive treatment) on patients, others opt for non-surgical medical (conservative) treatment. With such a high rate of functional impairment,

surviving patients might also opt for palliative care (PC) instead of life-prolonging treatments. However, recommendations for optimal delivery of PC is also lacking. As a result, physicians rely on discretionary decision-making that is sensitive to physicians' characteristics and healthcare resources. Our work suggested that age alone should not be the reason to deny neurosurgical procedures, and better prognostic markers are required to support treatment decisions in elderly patients with severe TBI. Current medications, illnesses, and other physical characteristics should all be factored into the decision making process, as they impact the efficacy of the treatment as well as the recovery process.

From the results, it is evident that aggressive surgical treatment can reduce death and increase likelihood of favourable outcomes [2,5,6]. Even for the study that reported higher mortality rate in the aggressive (surgical) treatment group, the authors acknowledged that carefully selected elderly patients can benefit from neurosurgeries [3]. Although more research will need to be done in this area, this promises good outcomes for TBI elderly patients. Considerations include presence of coagulopathy, level of consciousness, GCS score, radiologic type of injury, injury mechanisms, and CT scan results [3,5]. Delayed surgeries might also be more beneficial compared to early surgeries [6]. This means that there exists a timeline in which surgery may or may not be beneficial, but this again allows evidence for the benefits of aggressive treatment. This finding of delayed surgeries having more benefits than early surgery is a rare finding and has not been found in many other studies involving neurological intervention. Thus, this is a future area of research and this study should be taken cautiously. Despite this, in severe conditions with high mortality in which aggressive treatment should not be used and conservative treatment comes into play, the results show that PC should be utilized. Evidence suggests that PC utilization does not compromise survival and early initiation of PC reduces non beneficial support and healthcare costs [7,8,9]. This means that integrating PC into a standard treatment protocol can be beneficial. Early PC consultations that involve family meetings about end-of-life care goals and priorities can better manage expectations and minimize ordeal [10]. This can improve upon the patientdoctor relationship, and improve the patient's quality of life. In this light, we recommend discussion with healthcare providers in advance about conditions for treatment termination in case of traumas to facilitate implementation of palliative care.

One major limitation in this study includes the small subset of patients, as evident in the study done by Wan et al. (n < 115), Lilley et al. (n < 100), and Wu et al. (n < 24 for patients that received PC) [2,7,8]. With such a limited sample size of patients, the findings may be inaccurate or not representative of the elderly population receiving these treatments. Although these are observational studies and thus, it is harder to control the number of participants, it is

important to have a higher number of patients in each category in order to discover significant results. Future studies should look into the different aggressive treatments. Although in this study, there were a few types of surgical intervention included, it is important to determine exactly which surgeries are the most effective for elderly TBI patients. This can create more precise guidelines and help physicians determine the best and personalized treatment plan for their patient. Furthermore, one type of surgical treatment may be beneficial to a certain group of elderly individuals, while another surgery might be better for another group. Large prospective studies are also required to assess and confirm findings.

Conclusions

Overall, age should not be the only determining factor for treatment decisions. It is possible that carefully selected elderly TBI patients can benefit from neurosurgeries. However, these individuals must have various key factors and the severity of their TBI also comes into play. If aggressive surgery is not possible for the patient, integrative palliative care can also improve quality of life for both patients and their family without compromising survival. The patient's symptoms may be relieved while mortality risks do not increase. As determined in this review, various factors, such as GCS score and medical history, can predict the outcome of a TBI treatment. Future research should investigate prognostic markers to support treatment decisions, as it is important to create a comprehensive guideline on TBIs and their treatment. This is because elderly people are often overlooked when deciding their ability to withstand aggressive treatment or any other treatment outside the norm. However, as demonstrated in this study, age is not, and should never be, the sole factor in a treatment decision.

List of Abbreviations Used

TBI: traumatic brain injury PC: palliative care

Conflicts of Interest

The authors declare they have no conflict of interests.

Ethics Approval and/or Participant Consent

MP: made substantial contributions to the design of the study, the collection of data as well as interpretation and analysis of the data, revised the manuscript critically, and gave final approval of the version to be published. NM: made substantial contributions to the design of the study, the collection of data as well as interpretation and analysis of the data, revised the manuscript critically, and gave final approval of the version to be published.

Acknowledgements

This article acknowledges Olivia Tong, BSc and a Masters Candidate, for her help in the research, organization, and editing of this paper.

Funding

This study was not funded.

References

- Thompson HJ, McCormick WC, Kagan SH. Traumatic brain injury in older adults: epidemiology, outcomes, and future implications. Journal of the American Geriatrics Society. 2006 Oct;54(10):1590-5. http://dx.doi.org/10.1111/j.1532-5415.2006.00894.x
- [2] Wan X, Liu S, Wang S, Zhang S, Yang H, Ou Y, Zhao M, James L, Shu K, Chen J, Lei T. Elderly patients with severe traumatic brain injury could benefit from surgical treatment. World neurosurgery. 2016 May 1;89:147-52. <u>http://dx.doi.org/10.1016/j.wneu.2016.01</u>.084
- [3] Herou E, Romner B, Tomasevic G. Acute traumatic brain injury: mortality in the elderly. World neurosurgery. 2015 Jun 1;83(6):996-1001. <u>http://dx.doi.org/10.1016/j.wneu.2015.02.023</u>
- [4] Skaansar O, Tverdal C, Rønning PA, Skogen K, Brommeland T, Røise O, Aarhus M, Andelic N, Helseth E. Traumatic brain injury—the effects of patient age on treatment intensity and mortality. BMC neurology. 2020 Dec;20(1):1-0. <u>http://dx.doi.org/</u> <u>10.1186/s12883-020-01943-6</u>
- [5] Wutzler S, Lefering R, Wafaisade A, Maegele M, Lustenberger T, Walcher F, Marzi I, Laurer H, TraumaRegister DGU. Aggressive operative treatment of isolated blunt traumatic brain injury in the elderly is associated with favourable outcome. Injury. 2015 Sep 1;46(9):1706-11. <u>http://dx.doi.org/10.1016/j.injury.2015</u>.02.013
- [6] Laic RA, Sloten JV, Depreitere B. Neurosurgical treatment in elderly patients with Traumatic brain injury: A 20-year follow-up study. Brain and Spine. 2023 Jan 1;3:101723. <u>https://doi.org/10.1016/j.bas</u>. 2023.101723
- [7] Lilley EJ, Scott JW, Weissman JS, Krasnova A, Salim A, Haider AH, Cooper Z. End-of-life care in older patients after serious or severe traumatic brain injury in low-mortality hospitals compared with all other hospitals. JAMA surgery. 2018 Jan 1;153(1):44-50. http://dx.doi.org/10.1001/jamasurg.2017.3148
- [8] Wu A, Zhou J, Quinlan N, Dirlikov B, Singh H. Early palliative care consultation offsets hospitalization duration and costs for elderly patients with traumatic brain injuries: Insights from a Level 1 trauma center. Journal of Clinical Neuroscience. 2023 Feb 1;108:1-5. http://dx.doi.org/10.1016/j.jocn.2022.12.013

- [9] Hwang F, Pentakota SR, Glass NE, Berlin A, Livingston DH, Mosenthal AC. Older patients with severe traumatic brain injury: national variability in palliative care. Journal of surgical research. 2020 Feb 1;246:224-30. <u>http://dx.doi.org/10.1016/j.jss.2019.09</u> .002
- [10] Lilley EJ, Williams KJ, Schneider EB, Hammouda K, Salim A, Haider AH, Cooper Z. Intensity of treatment, end-of-life care, and mortality for older patients with severe traumatic brain injury. Journal of Trauma and Acute Care Surgery. 2016 Jun 1;80(6):998-1004. http://dx.doi.org/10.1097/TA.000000000001028

Article Information

Managing Editor: Jeremy Y. Ng Peer Reviewers: Olivia Tong, Regina Annirood Article Dates: Received Aug 03 23; Accepted Sep 25 23; Published Oct 18 23

Citation

Please cite this article as follows: Patel MH, Mehta ND. Evaluating the efficacy of aggressive treatments and palliative care for traumatic brain injuries in elderly patients: A review. URNCST Journal. 2023 Oct 18: 7(10). <u>https://urncst.com/index.php/urncst/article/view/527</u> DOI Link: <u>https://doi.org/10.26685/urncst.527</u>

Copyright

© Mukti H. Patel, Nidhi D. Mehta. (2023). Published first in the Undergraduate Research in Natural and Clinical Science and Technology (URNCST) Journal. This is an open access article distributed under the terms of the Creative Commons Attribution License (<u>https://creativecommons.org/licenses/by/4.0/</u>), which permits unrestricted use, distribution, and reproduction in any medium, provided the original work, first published in the Undergraduate Research in Natural and Clinical Science and Technology (URNCST) Journal, is properly cited. The complete bibliographic information, a link to the original publication on <u>http://www.urncst.com</u>, as well as this copyright and license information must be included.



Funded by the Government of Canada



Do you research in earnest? Submit your next undergraduate research article to the URNCST Journal! | Open Access | Peer-Reviewed | Rapid Turnaround Time | International | | Broad and Multidisciplinary | Indexed | Innovative | Social Media Promoted | Pre-submission inquiries? Send us an email at <u>info@urncst.com</u> | <u>Facebook</u>, <u>Twitter</u> and <u>LinkedIn</u>: @URNCST Submit YOUR manuscript today at <u>https://www.urncst.com</u>!