

PEER REVIEW HISTORY

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ARTICLE DETAILS

TITLE (PROVISIONAL)	Acute and long-term clinical, neuropsychological, and return-to-work sequelae following electrical injury: a retrospective cohort study
AUTHORS	Radulovic, Nada; Mason, Stephanie; Rehou, Sarah; Godleski, Matthew; Jeschke, Marc

VERSION 1 – REVIEW

REVIEWER	Marijon, Eloi Paris Cardiovascular Research Center
REVIEW RETURNED	20-Aug-2018

GENERAL COMMENTS	<p>This study identifies and delineates common sequelae that extend beyond acute management. EIs are implicated in multifaceted clinical, neuropsychological and social sequelae. Effects exist acutely and long-term, warranting monitoring that extends beyond initial treatment. Low voltage injuries are, at minimum, as likely as high voltage ones of exhibiting complications during recovery. Lastly, the authors have identified these effects as possible barriers for successful employment reintegration. Collectively, these findings indicate a need for focused training and rehabilitation. The authors should be congratulated to this important and new contribution. I would only suggest minor things, including an update of the recent literature on this point (excellent review paper recently published that could be considered in the Introduction- Waldmann V et al. Eur Heart J 2018), and also the need to educate the public (to extent in the Discussion section) to avoid electrical injury such as this educational paper published in the BMJ Group journal (PMID: 28404561). Also, because of the absence of control group, any causality between EIs and neuropsychological sequelae should be considered with caution. Again, congratulations for the excellent work.</p>
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REVIEWER	Hamid Karimi M.D. Professor of Plastic Surgery, Iran University of Medical Sciences, Iran
REVIEW RETURNED	29-Aug-2018

GENERAL COMMENTS	<ol style="list-style-type: none">1. Abstract; you mentioned: "Sixty-one percent returned to their pre-injury employment and 19% were unable to return to any form of work" what about the rest of them?2. Results; 2nd paragraph; you mentioned: "the incidence of inhalation injury was low", It is usual to have inhalation injury during Electrical injury? Please explain.
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	<p>3, Table 1; Number of patients for rehabilitation were more in low voltage group. How you explain it?</p> <p>4. Table 1; what were the causes for mortality in your patients?</p> <p>5. Table 2; the number of patients with psychological problems before 5 years were higher in low voltage group, and the number of patients who got treatments and medications, how do you explain it?</p> <p>Meanwhile in page 17 you have written :” Voltage groups did not differ in their rates of treatment and medication requirements for management of neuropsychological sequelae.” ???</p> <p>6. In page 18:” A similar inability to return to any form of employment was observed between voltage groups” and in page 19:” LVIs are more commonly associated with unsuccessful RTW.” Please explain !</p> <p>7. Some other papers about long term sequelae of electrical injuries can be used. Such as :</p> <ul style="list-style-type: none"> - Noor-Ahmad Latifi , Hamid Karimi, Acute electrical injury: A systematic review Journal of acute disease 2017, 6 (3), 93-96 - H Karimi, M Momeni, M Vasigh, Long term outcome and follow up of electrical injury Journal of Acute Disease 2015, 4 (1), 111-117
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REVIEWER	Dr Edward Watson Chelsea and Westminster Hospital NHS Foundation Trust, Magill Department of Anaesthesia, Intensive Care & Pain Management
REVIEW RETURNED	04-Sep-2018

GENERAL COMMENTS	<p>Dear Professor Jeschke,</p> <p>This is an interesting paper that seeks to demonstrate the differential effect of low- and high-voltage electrical injuries as well as comparing the acute- and longer-term effects. You have shown that high voltage injuries produce more acute sequelae than low voltage injuries, and that the long-term psychological impact of both high and low voltage injuries is a significant burden.</p> <p>This retrospective cohort study adds to current published data set. Many have shown the impact the acute sequelae of electrical burns, but there are no studies which also look to profile the long-term outcomes. As such, this paper is important for service provision planning, but it also raises many further questions and acts as a hypothesis generating tool to inspire future research avenues.</p> <p>There was a lot of data presented in the paper with reference to multiple sub-cohorts or varying sizes. At times this was confusing on the first read through. It may help readers to place the patient flow diagram (Supplementary figure 1) within the results section for easy reference, rather than as online supplementary material. It would also be helpful to add the acute cohorts to the diagram (101 discharged without rehab, 106 requiring rehab, 59 acute neuropsychological data with 4 excluded). Lastly, a few minor amendments might help to clarify some particulars of the methodology:</p> <p>Page 7, Line 24 Consider citing a source for the delineation between HVI and LVI</p>
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	<p>If the definition of voltage is based on IEC 60038:1983, then it would be important to highlight that this is defined by arcing risk. Considering the majority of participants are occupational, and many involved overhead cables, it would be helpful to reference the standard Mains voltage and overhead cable voltage for your region.</p> <p>Page 9, Line 10 Please provide the rationale for the start date of November 1998</p> <p>Page 9, Line 12 Did all patients have a documented voltage?</p> <p>Page 9, Line 40 TBSA does not typically have a normal distribution, and should be presented as median and IQR as per the statistical analysis section on page 11. The mean of 8 and SD of 12 suggests a non-normal distribution.</p> <p>Page 9, Line 45 Do the RTBC records specify flame involvement?</p> <p>Page 9, Line 51 EI is notorious for inflicting a relatively low surface injury, as such LOS/%TBSA seems like an unreliable outcome measure. You may wish to explore the limitations of this outcome measure in the discussion.</p> <p>Page 9, Line 49 For patients discharge to inpatient rehab, was this time included in their LOS, or was it limited to their admission to RTBC?</p> <p>Page 10, Line 8 Please state who performs the neuropsychological screening, was it purely observational or did it involve a formal or semi-formal interview?</p> <p>Page 10, Line 17 What form did the screening tool take? Was it a tick-box form, Leikert scale or open box response?</p> <p>Page 10, Line 31 There is propensity for confusion throughout the paper with multiple references to psychological symptoms (e.g. anxiety) and psychological diagnoses (e.g. GAD). It is important to clarify each section by labelling anxiety and depressed mood as symptoms.</p> <p>Page 12, Line 45 LOS/%TBSA is reported as parametric data but the values suggest a non-normal data set.</p> <p>Page 13, table 1 It would be useful to have TBSA listed in the row below LOS/%TBSA for easy comparison</p> <p>Page 13, table 1 % requiring rehabilitation is the only outcome that is worse in the LVI group, but is not mentioned in the positive findings in the discussion.</p> <p>Page 13, table 1 'Discharged to outpatient rehabilitation' has a p value of >.99, which seems unusual given the large discrepancy between HVI and LVI.</p> <p>Page 14, table 2 'Days to first follow up': please clarify if this is from date of injury.</p> <p>Page 15, line 3 Number of operations should also be listed here (p<0.001) as an outcome measure from the methodology section.</p>
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	<p>Page 15 paragraph 2 This would be more clearly summarised by stating that there was no significant difference between HVI and LVI for any symptom, with the data moved to Figure 1.</p> <p>Page 16, line 10 Clarify if time to psychiatric diagnosis is from date of injury or date of admission to SJRH</p> <p>Page 16, line 17 Clarify what is meant by 'Of the majority of patients, 81% experienced...'</p> <p>Page 16, line 26 Clarify whether 60% refers to the entire cohort of 122 patients, or of those who displayed symptoms.</p> <p>Page 16, line 42 If available, please consider providing the reason for the missing data (percentage not-recorded, percentage still in follow up etc.)</p> <p>Page 17, line 3 Specify RTW is from date of injury</p> <p>Page 17, line 48 It is unclear if this is referring to the treatment of psychological symptoms or psychological diagnoses.</p> <p>Page 17, line 48 The methodology is not stated: does rate of treatment refer to number of days receiving treatment or number of patients receiving treatment. Also, does medication requirements refer to number of patients requiring medication, number of days requiring treatment or number of medications required?</p> <p>Page 19, line 10 Neuropsychological symptoms did increase from the acute admission to the rehabilitation period, however, the data also show that they reduced after 5 years.</p> <p>Page 19, line 15 Please specify greater rates of psychological symptoms</p> <p>Page 19, line 24 %RTW for LVI vs HVI did not reach significance (Table 3, p=0.43)</p> <p>Page 20, line 8 This sentence implies that executive function was assessed in this study</p> <p>Page 20, line 24 I felt that it needs to be noted that the Meyer population was half the age of this cohort and a more equal gender mix. There is also typically a much higher premorbid mental health burden in the general burns population, where as electrical injuries tend to be accidental occupational exposure.</p> <p>Page 21, line 26 It seems pertinent to the outcome measures that a psychologist should be included in the multi-disciplinary team.</p> <p>This is some very interesting data and an important publication, but a bit of extra detail will help to clarify the methodology.</p>
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VERSION 1 – AUTHOR RESPONSE

Response to Reviewers

Reviewer #1

This study identifies and delineates common sequelae that extend beyond acute management. EIs are implicated in multifaceted clinical, neuropsychological and social sequelae. Effects exist acutely and long-term, warranting monitoring that extends beyond initial treatment. Low voltage injuries are, at minimum, as likely as high voltage ones of exhibiting complications during recovery. Lastly, the authors have identified these effects as possible barriers for successful employment reintegration. Collectively, these findings indicate a need for focused training and rehabilitation. The authors should be congratulated to this important and new contribution. I would only suggest minor things, including an update of the recent literature on this point (excellent review paper recently published- that could be considered in the Introduction- Waldmann V et al. Eur Heart J 2018), and also the need to educate the public (to extent in the Discussion section) to avoid electrical injury such as this educational paper published in the BMJ Group journal (PMID: 28404561). Also, because of the absence of control group, any causality between EIs and neuropsychological sequelae should be considered with caution. Again, congratulations for the excellent work.

Thank you very much for your feedback and suggestions. We have now clarified the limitations of our study with respect to identifying causal relationships between EIs and neuropsychological sequelae (Pg. 22), and have additionally included the recommended papers into our introduction and discussion sections.

Reviewer #2

1. Abstract; you mentioned: “Sixty-one percent returned to their pre-injury employment and 19% were unable to return to any form of work” what about the rest of them?

Thank you for this question. The results in the abstract provide a brief summary of our findings due to word limitations, which are further elaborated upon in the main results section of the manuscript. Regarding RTW, 61% returned to pre-injury employment, 19% were unable to return to any form of work, and the remaining 19% returned to alternative employment through labour market re-entry. These points are addressed on Pg. 17.

2. Results; 2nd paragraph; you mentioned:” the incidence of inhalation injury was low”, It is usual to have inhalation injury during Electrical injury? Please explain.

We evaluated certain outcomes that are prevalent amongst the general burn population, including inhalation injury, for the purpose of contrasting EI outcomes relative to this general population. However, our findings, including a low incidence of inhalation injury, indicate that this particular outcome is not common in the EI population. Inhalation injury in EI can occur by an EI arc type injury, but again, it is very rare.

3, Table 1; Number of patients for rehabilitation were more in low voltage group. How you explain it?

The proportion of patients in the LVI group requiring rehabilitation is lower than the proportion of HVI patients. This may be attributed to the increased rates of complications and amputations observed following HVIs when contrasted with the clinical course of LVIs. However, the percentage of LVI patients directly discharged to outpatient rehabilitation following treatment at *RTBC* is greater than that of the HVI group. This is likely a result of more HVI patients requiring inpatient rehabilitation following acute treatment, resulting in fewer HVI patients being directly discharged to outpatient rehabilitation.

4. Table 1; what were the causes for mortality in your patients?

These are the indicated causes of mortality for the four patients who died post-EI: 1) Anoxia, 2) ARDS and SIRS, 3) Sepsis, 4) Massive burns.

5. Table 2; the number of patients with psychological problems before 5 years were higher in low voltage group, and the number of patients who got treatments and medications, how do you explain it? Meanwhile in page 17 you have written :” Voltage groups did not differ in their rates of treatment and medication requirements for management of neuropsychological sequelae.” ???

It is quite interesting the LVI have so many mental health issues. We are also surprised by the high incidence of these sequelae. The cause is not entirely clear, but we speculate that a HVI is more like a profound trauma with immediate responses and recognized as such. In contrast, a LVI is subtle and not always recognized. As such, underlying mental health and physiological issues will not be immediately treated. To us, it appears to be a matter of intervention and treatment, but this is purely speculative. This has been added to the manuscript.

6. In page 18:” A similar inability to return to any form of employment was observed between voltage groups” and in page 19:” LVIs are more commonly associated with unsuccessful RTW.” Please explain !

Thank you for this feedback. We have now revised our statement on Pg. 19 to clarify this. While our findings indicate that LVIs result in slightly greater rates of unsuccessful RTW, these results are not statistically significant when compared to HVI. Therefore, while some slight differences are noted, both voltage groups result in a similar inability to return to employment, which is very concerning.

7. Some other papers about long term sequelae of electrical injuries can be used. Such as :

- Noor-Ahmad Latifi , Hamid Karimi, Acute electrical injury: A systematic review
Journal of acute disease 2017, 6 (3), 93-96
- H Karimi, M Momeni, M Vasigh, Long term outcome and follow up of electrical injury
Journal of Acute Disease 2015, 4 (1), 111-117

Thank you for these suggestions, both are very fitting papers for this topic.

Reviewer #3

This is an interesting paper that seeks to demonstrate the differential effect of low- and high-voltage electrical injuries as well as comparing the acute- and longer-term effects. You have shown that high voltage injuries produce more acute sequelae than low voltage injuries, and that the long-term psychological impact of both high and low voltage injuries is a significant burden.

This retrospective cohort study adds to current published data set. Many have shown the impact the acute sequelae of electrical burns, but there are no studies which also look to profile the long-term outcomes. As such, this paper is important for service provision

planning, but it also raises many further questions and acts as a hypothesis generating tool to inspire future research avenues.

There was a lot of data presented in the paper with reference to multiple sub-cohorts or varying sizes. At times this was confusing on the first read through. It may help readers to place the patient flow diagram (Supplementary figure 1) within the results section for easy reference, rather than as online supplementary material. It would also be helpful to add the acute cohorts to the diagram (101 discharged without rehab, 106 requiring rehab, 59 acute neuropsychological data with 4 excluded). Lastly, a few minor amendments might help to clarify some particulars of the methodology:

Thank you for your suggestions. Unfortunately, we have reached the maximum number of figures/tables for our main manuscript and are therefore required to include the flow diagram into the supplement document. However, we have modified the diagram accordingly, based on your recommendation - it now includes the number of patients in the acute cohort who did and did not require rehabilitation. Acute neuropsychological data and the study exclusion were already part of our study.

Page 7, Line 24 Consider citing a source for the delineation between HVI and LVI. If the definition of voltage is based on IEC 60038:1983, then it would be important to highlight that this is defined by arcing risk. Considering the majority of participants are occupational, and many involved overhead cables, it would be helpful to reference the standard Mains voltage and overhead cable voltage for your region.

Thank you for this note. We have now clarified the basis of HVI and LVI classification according to arcing risk on Pg. 5.

Page 9, Line 10 Please provide the rationale for the start date of November 1998

This is the date of when RTBC was first established at Sunnybrook Health Sciences Centre, and thus, is the earliest date for available health records. This has now been clarified in the paper on Pg. 8.

Page 9, Line 12 Did all patients have a documented voltage?

A total of nine patients did not have a specified injury voltage in their medical record. This has now been addressed in the Results section under "Acute period: Demographics" on Pg. 12.

Page 9, Line 40 TBSA does not typically have a normal distribution, and should be presented as median and IQR as per the statistical analysis section on page 11. The mean of 8 and SD of 12 suggests a non-normal distribution.

Thank you. This has now been addressed in Table 1 and in other relevant sections.

Page 9, Line 45 Do the RTBC records specify flame involvement?

RTBC records do specify flame involvement. However, all of our cohort either sustained a contact injury, a flash injury, or a lightning injury, all of which are addressed in Supplementary Table 1.

Page 9, Line 51 EI is notorious for inflicting a relatively low surface injury, as such LOS/%TBSA seems like an unreliable outcome measure. You may wish to explore the limitations of this outcome measure in the discussion.

Thank you for your suggestion. We have now explored this limitation in the discussion section, on Pg. 21.

Page 9, Line 49 For patients discharge to inpatient rehab, was this time included in their LOS, or was it limited to their admission to RTBC?

This time was not included in their LOS (as it was limited to their stay at *RTBC*). This detail has now been specified on Page 9.

Page 10, Line 8 Please state who performs the neuropsychological screening, was it purely observational or did it involve a formal or semi-formal interview?

Thank you. This screen was done by the care team at *RTBC* as part of the referral documentation.

We have revised our methods on Pg. 9 to indicate this.

Page 10, Line 17 What form did the screening tool take? Was it a tick-box form, Leikert scale or open box response?

This neuropsychological screen as part of the referral process was observational in nature. We have now clarified this in the methods section on Pg. 9.

Page 10, Line 31 There is propensity for confusion throughout the paper with multiple references to psychological symptoms (e.g. anxiety) and psychological diagnoses (e.g. GAD). It is important to clarify each section by labelling anxiety and depressed mood as symptoms.

Thank you. This has now been clarified on Pg. 9.

Page 12, Line 45 LOS/%TBSA is reported as parametric data but the values suggest a non-normal data set.

Thank you. We have revised the way in which we have reported this parameter.

Page 13, table 1 It would be useful to have TBSA listed in the row below LOS/%TBSA for easy comparison

We have now modified Table 1 to include %TBSA.

Page 13, table 1 % requiring rehabilitation is the only outcome that is worse in the LVI group, but is not mentioned in the positive findings in the discussion.

The percentage of patients requiring any form of rehabilitation is greater following HVI vs. LVI (65% vs. 44%) (Table 1).

Page 13, table 1 'Discharged to outpatient rehabilitation' has a p value of >.99, which seems unusual given the large discrepancy between HVI and LVI.

Thank you. We have now modified our proportions to be analyzed based on the total number of patients receiving rehabilitation in each group, as oppose to the entire patient cohort. Please refer to the footnote of Table 1 for more details. The newly calculated p-value is $P=.005$.

Page 14, table 2 'Days to first follow up': please clarify if this is from date of injury. The table has been revised to include clarification in the footnotes. Days to follow-up were calculated based on the date of injury.

Page 15, line 3 Number of operations should also be listed here (p<0.001) as an outcome measure from the methodology section.

Thank you, this has now been included.

Page 15 paragraph 2 - This would be more clearly summarised by stating that there was no significant difference between HVI and LVI for any symptom, with the data moved to Figure 1.

Thank you, we have attempted to revise this paragraph accordingly.

Page 16, line 10 Clarify if time to psychiatric diagnosis is from date of injury or date of admission to SJRH

Thank you. Time to psychiatric diagnosis has been clarified on Page 16 as being from the date of injury.

Page 16, line 17 Clarify what is meant by ‘Of the majority of patients, 81% experienced...’ This sentence has now been revised to read “Additionally, eighty-one percent of long-term cohort...” on Pg. 15. Thank you for pointing out this area of confusion.

Page 16, line 26 Clarify whether 60% refers to the entire cohort of 122 patients, or of those who displayed symptoms.

The 60% refers to the entire long-term cohort of 122 patients. This has now been clarified on Pg.

15.

Page 16, line 42 If available, please consider providing the reason for the missing data (percentage not-recorded, percentage still in follow up etc.)

We have now clarified on Pg. 15 that this was due to data not being recorded for that portion of the cohort.

Page 17, line 3 Specify RTW is from date of injury

Time to RTW has now been clarified as being from the time of injury, on Page 16.

Page 17, line 48 It is unclear if this is referring to the treatment of psychological symptoms or psychological diagnoses.

Thank you. We have clarified this on Pg. 17. Additionally, we have defined sequelae as encompassing symptoms and diagnoses in the methods section.

Page 17, line 48 The methodology is not stated: does rate of treatment refer to number of days receiving treatment or number of patients receiving treatment. Also, does medication requirements refer to number of patients requiring medication, number of days requiring treatment or number of medications required?

Rates of these parameters have now been defined in the “Methods” section (Pg. 9) as the percentage of patients requiring these types of treatment modalities.

Page 19, line 10 Neuropsychological symptoms did increase from the acute admission to the rehabilitation period, however, the data also show that they reduced after 5 years. Thank for

you for this important note - we have now revised our statement on Pg. 18 to reflect the decline in rates of neuropsychological symptoms that is observed in our long-term cohort.

Page 19, line 15 Please specify greater rates of psychological symptoms Thank you. We have now specified exact rates in the results section on Pg. 16.

Page 19, line 24 %RTW for LVI vs HVI did not reach significance (Table 3, p=0.43). While we did note that these differences were comparable, we have now additionally specified on Pg. 19 that they are not statistically significant. We have also indicated that the differences in rate or RTW are marginal. Despite this, we have chosen to keep the part of our discussion that notes the small differences in RTW rates between voltage groups, as we would like to highlight ways in which the underappreciated LVIs may be implicated in similar, or potentially worse, outcomes. Additionally, we feel that these rates are concerning regardless of statistical significance, as they can have profound socioeconomic impacts.

Page 20, line 8 This sentence implies that executive function was assessed in this study We have revised the sentence accordingly on Pg. 19 to prevent any confusion regarding the outcomes assessed by our study.

Page 20, line 24 I felt that it needs to be noted that the Meyer population was half the age of this cohort and a more equal gender mix. There is also typically a much higher premorbid mental health burden in the general burns population, where as electrical injuries tend to be accidental occupational exposure.

Thank you. This important clarification of the cohort differences between studies has been noted on Pg. 19.

Page 21, line 26 It seems pertinent to the outcome measures that a psychologist should be included in the multi-disciplinary team.

Thank you for this note. Our findings certainly suggest the vital role of psychologists in the rehabilitation of EI patients. Our previous statement on Page 20 has now been revised to reflect this.

This is some very interesting data and an important publication, but a bit of extra detail will help to clarify the methodology.

Thank you very much.

VERSION 2 – REVIEW

REVIEWER	Hamid Karimi Iran University of Medical Sciences, Tehran, Iran
REVIEW RETURNED	23-Dec-2018
GENERAL COMMENTS	It is now suitable for publication