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REVIEW

Pressure ulcer risk factors in persons with spinal cord injury Part 2: the chronic stage

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Introduction: Pressure ulcers (PUs) are a common complication following spinal cord injury (SCI). Prevalence for persons in the chronic SCI stage varies between 15 and 30%. The risk assessment scales used nowadays were designed on pathophysiological concepts and are not SCI-specific. Recently, an epidemiological approach to PU risk factors has been proposed for designing an SCI-specific assessment tool. The first results seem quite disappointing, probably because of the level of evidence of the risk factors used.
Objective: To determine PU risk factors correlated to the chronic stage of SCI.
Materials and methods: Systematic review of the literature.
Results: There are several PU risk factors for chronic SCI stage: socio-demographics, neurological, medical or behavioral. The level of evidence varies: it is quite high for the socio-demographics and neurological factors and low for behavioral factors.
Discussion and conclusion: Behavioral risk factors (relieving the pressure, careful skin monitoring, smoking) are probably the ones for which a preventive strategy can be established. It is important to develop specific assessment tools for these behavioral risk factors to determine their relevance and evaluate the effect of therapeutic educational programs on persons with SCI.
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Pressure ulcers (PUs) are now the most common complication for persons with spinal cord injury (SCI),[1,2] despite the large number of recommendations available for information and prevention and the technological progress made for preventing and treating PU. PU have become the second cause of rehospitalization after an SCI,[3] with estimated annual costs amounting to $1.4 billion in the United States.[4]

During the acute stage, meaning before the patient's admission to a Physical Medicine and Rehabilitation (PM&R) Center, 21–37% of SCI patients go on to develop a PU.[5,6] The PM&R stay does not seem to be a risk period as only 2% of SCI patients leaving a rehabilitation center for a first-time PM&R care are affected by a PU.[7] PU prevalence in chronic SCI stage varies from 15 to 30%. The risk factors during these different stages are probably not the same.[8]

The goal of this systematic literature review is to evaluate today's knowledge on PU risk factors in SCI patients at each stage of their specific care.

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The first part of this work focused on the acute and PM&R stages of a SCI patient's care and were reported earlier.[9] The risk factors for acute SCI patients are essentially linked to the care management and duration of hospitalization stays. Clinical factors do not seem to have an effect. The literature is too scarce to define precisely the PU risk factors in PM&R units or centers.

In this second part we will focus on the PU risk factors for persons with chronic SCI.

Materials and methods

The methodology used for our review was conducted according to the recommendations from the Cochrane Library[10] and was detailed earlier.[9]

Results

Results from the bibliographical search
The databases search found 820 references. The first analysis from the titles and abstracts kept 40 articles. The references analysis allowed adding of two additional articles. The second analysis based on the full text excluded 20 articles.

Among the 22 studies selected, six studies focused on acute SCI patients (pre-hospital stay or in neurosurgery care). Two studies were conducted during the PM&R stage and 14 in chronic SCI patients.

PU-related risk factors in chronic SCI patients

The literature analysis reported 14 articles focusing on chronic SCI patients (Table 1).

Among these articles we find four cohort studies[11–14] including one historical cohort,[14] one case–control study[15] and nine cross-sectional studies.[4,16–23] The study by Krause *et al*.[19] seemed at first to use a case–control design but is in fact a cross-sectional study. The cohort studies by Chen *et al*.[11] and Mac Kinley *et al*.[13] focus on the same cohort from National Spinal Cord Injury Database but with a few years time gap. It seems highly likely that the data are similar in both studies.

The mean score for methodological quality is 64.7% ($E = 42.8–82.1$). The number of patients included varied from 118 to 6776[13] with a total number of 15,827. The studies that included the largest number of patients[11,13] are also those with the best methodological level.

Pressure ulcers (PUs) were clinically and directly evaluated in seven studies and by questionnaire in seven other studies.

The literature search found 40 risk factors that were studied and could be classified as such:

Socio-demographic factors (Table 2). *Sex* was accounted for in eight studies. No cross-sectional study found a link with the onset of a PU.[4,17,19–21] Being male was found to be a risk factor in two high-power cohort studies, thus validating this risk factor with a strong level of evidence.[11,13] The odds ratio (OR) was evaluated at 1.3 (95% CI = 1.1–1.7).

Age is not a PU risk factor for the chronic SCI patient. This was validated by cross-sectional[4,17,20,21] or cohort studies.[11–14] There was strong level of evidence.

Ethnicity is a controversial risk factor, but it was only reported in one cohort study conducted in the United States.[11] There might be some confusing factors, mainly socio-economic, which are specific to African-American populations in the United States. Thus it seems impossible to extrapolate this factor for the rest of the world.

The results regarding *marital status* are conflicting in several cross-sectional studies.[4,17,18] A cohort study with a good methodological level[11] considers that being married is a protective factor (OR = 0.7; 95% CI = 0.6–0.8). The level of evidence is moderate.

A low *educational achievement level* is linked to PU prevalence in cross-sectional studies,[18,21] and is a risk factor in a cohort study[11] (OR = 1.3; 95% CI = 1.1–1.5). This factor has not been identified in another cohort study with a lower methodological quality.[12] The level of evidence is moderate.

Unemployment is linked to PU prevalence in several cross-sectional studies,[18–21] except the one by Raghavan *et al*.[17] The cohort study by Chen *et al*.[11] indirectly confirms this relationship by showing that being employed or a student is a protective factor with an odds ratio evaluated at 0.7 (95% CI = 0.6–0.9). Two other cohort studies with a lower methodological quality do not report this correlation. The level of evidence is moderate.

Neurological factors (Table 2). *Young age at the time of the injury* is a PU-related risk factor in a cross-sectional study[12,21] and a cohort study with higher methodological quality.[12] The level of evidence is moderate.

Time Since Injury is a PU-related factor in several cross-sectional studies[12,21,22] and is validated by three cohort studies.[12,13,24] Only the cross-sectional studies by Fuhrer *et al*.[4] and Krause[20] as well as the cohort study by Salzberg[14] do not confirm this causal relationship. We can consider that the PU risk increases with time since injury with a strong level of evidence.

The SCI *trauma etiology* is considered as a risk factor by a first cohort study.[13] This notion is undermined by a second cohort study,[11] which does not find this relationship, taking into account the multivariate analysis of the demographic factors described above. We cannot consider SCI etiology as a risk factor, with a moderate level of evidence.

Only one cross-sectional study associates the onset of PU with a cervical *injury level*.[20] Other cross-sectional[4,19,22] or cohort studies[11,13,14] do not report any link between injury level and the onset of a PU. The level of evidence is strong.

Transversal extension of the SCI, assessed by the ASIA or Frankel score, is a PU risk factor for chronic SCI patients found in two cohort studies,[11,13] one historical cohort[14] and two cross-sectional studies.[20,21] The level of evidence is strong. Odds ratios, according to Chen,[11] are 8 (95% CI = 5.6–11.3) for an ASIA A score of 6 (95% CI = 4.1–8.8) for an ASIA B score and 3 (95% CI = 2.1–4.4) for an ASIA C score. According to the cross-sectional study by Sumiya *et al*.,[16] there is no correlation between PU and sensibility disorders at the seating level.

Vertical extension of the SCI, assessed by the ASIA Motor Index, is a suggested risk factor in one cross-sectional study[4] and is validated by a cohort study.[12] The level of evidence is moderate.

Medical and biological factors (Table 3). Several medical pathologies associated with SCI have been studied. The results with regard to the cardiovascular pathologies are discordant and were evaluated in studies with a methodological level that was too low[14,15] to come to any conclusions. These studies also assessed the effect of diabetes mellitus, without finding any correlation. The level of evidence is insufficient. Other intercurrent pathologies were identified as risk factors in two cohort studies with a very good methodological level.[11,13] The level of evidence is strong for deep venous thrombosis and infectious pneumopathy, and moderate for fractures of the lower limbs and autonomic dysreflexia.

Only one retrospective cohort study[14] evaluated the effect of low albumin levels on the onset of PU and found a significant relationship. The level of evidence is insufficient.

Impairment and disability. Impairment, assessed by the FIM scale, is a risk factor suggested by a cross-sectional study[4] and

Table 1 Results of observational studies assessing PU risk factors for chronic SCI patients

Study	*Design*	*Analysis type*	*Population*	*PU variable*	*Factors studied*	*Results*
Anderson[23]	Cross sectional Monocenter Date not available USA Quality Assessment: 46.4%	Multivariate	$N=141$ Traumatic SCI Male: 81% Tetraplegic: 59% Age: 34 years TSI: 10.4 years	Questionnaire	Prevention practice (RESPON questionnaire, not referenced) Quality of life (SATIS not referenced) Self esteem (Self-concept scale)	S: No PU is associated with patient prevention practice S: No PU is associated with quality of life NS
Fuhrer[4]	Cross sectional Multicenter USA Date not precised Quality Assessment: 67.8%	Univariate	$N=140$ Traumatic SCI Male: 71.4% Age: 36.2 years TSI: 10.6 years Tetraplegic: 50% ASIA A: 46%	Clinical evaluation Shea classification	TSI Lesion level Vertical extension (ASIA Motor Index score) Transversal extension (Frankel) Sex Age Ethnicity Marital status Educational level Disability (FIM scale) Handicap (CHART)	NS NS S NS NS NS NS NS NS S NS
Anson[22]	Cross sectional Monocenter USA Date not precised Quality Assessment: 53.6%	Univariate	$N=348$ Traumatic SCI Male: 82% Age: 37 years Tetraplegic: 57%	Clinical evaluation PU classification detailed but not referenced	TSI Lesion level	S NS
Niazi[15]	Case–control Monocenter From 1987 to 1993 USA Quality Assessment: 42.8%	Multivariate	$N=176$ (62 case and 114 controls)	Clinical evaluation (recurrence of initial PU) PU classification detailed but not referenced	Actual cigarette smoking Duration of smoking history Type of treatment of initial PU Cardiovascular disease Diabetes mellitus Level of activity (ambulatory-wheelchair use-confined to bed)	NS ($P=0.057$) S NS S NS S
Sumiya[16]	Cross sectional 1989 Monocenter Japan Quality Assessment: 46.4%	Univariate	$N=218$ Male: 92.2% Age: 43 years old TSI: 13.5 years Paraplegic: 100%	Questionnaire	Buttocks sensitive deficit Urinary incontinence General medical complications Skin self care prevention Physical activity	NS S NS S: patient with self-care practices have lower PU rate S (lack of regular physical activity is associated with the presence of PU)
Krause[20]	Cross sectional Multi center Quality Assessment: 71.4%	Univariate	$N=1017$ Male: 79% Age: 42 years old TSI: 13.3 years	Questionnaire Number of PU	Gender Ethnicity Lesion level Transversal extension (complete or not) Age Age at accident TSI Employment status	NS NS S: cervical level S: complete lesion NS NS NS S

Table 1 Continued

Study	*Design*	*Analysis type*	*Population*	*PU variable*	*Factors studied*	*Results*
Mc Kinley[13]	Cohort Multicenter 1973 to 1998 (National Spinal Cord Injury Database, USA) Quality Assessment: 82.1%	Univariate	$N=6776$ (TSI = 1 year) to $N=500$ (TSI 20 years)	Clinical evaluation Ennis and Sarmiento classification	TSI Age Gender Transversal extension (complete or not) Lesion level Etiology Associated secondary medical disorders	S NS S: male S NS S: traumatic etiology S: pneumonia, deep venous thrombosis, lower limb fracture, autonomic dysreflexia
Garber[12]	Cohort Date not available Multicenter Quality Assessment: 67.8%	Multivariate	$N=118$ to $N=100$ (3 years later)	Clinical evaluation PU scoring system not detailed	Age Ethnicity Marital status Education level Employment status Age at accident TSI Vertical extension (ASIA Motor Index) Disability (FIM) Handicap (CHART) PU medical history PU surgery history Health practice and belief (Health Belief Model) Daily skin monitoring	NS NS NS NS NS S PU and young age at accident S S S S S S S: self-assessed susceptibility to PU and presence of PU 3 years later S
Krause[18]	Cross sectional 1995 Multicenter (Arkansas SCI registry) Quality Assessment: 71.4%	Multivariate	$N=540$ Traumatic SCI Male: 76% Age: 44 years old TSI: 14.5 years	Questionnaire	Employment status Marital status Educational level General protective health behaviors[¥] (physical activity, healthy diet, healthy lifestyle) Skin-specific protective health behaviors[¥] (Turns frequently in bed, weight shifting, checks skin, keeps skin dry) Alcohol abuse Cigarette smoking Suicidal behavior	S (Currently employed OR = 0.69) S (Married OR = 0.52) S (16 or more years, OR = 0.30) NS NS[¥] NS S NS
Klotz[21]	Cross sectional Multicenter France 1993 Quality Assessment: 60.7%	Univariate	$N=1668$ Age = 43.6 years old TSI = 13 years Tetraplegic = 100%	Questionnaire	Age at time of the SCI Age Gender TSI Transversal extension (complete or incomplete) Educational level Employment status PU antecedent during acute stage	S, PU and young age at the time of the injury NS NS S S S S S

Table 1 Continued

Study	*Design*	*Analysis type*	*Population*	*PU variable*	*Factors studied*	*Results*
Raghavan[17]	Cross sectional Monocenter Date not available UK Quality Assessment: 82.1%	Multivariate	$N=472$ Traumatic SCI Male 76% Age: 47 years old	Questionnaire	Age Gender Professional status Marital status Current medical problems (yes/no) Cigarette smoking Bladder or bowel incontinence Daily skin monitoring Regular weight shifting (every hour)	NS NS NS NS S (OR = 1.8) S (OR = 1.8) NS S (OR = 0.5) NS
Krause[19]	Cross sectional[a] Monocenter USA Assessment: 82.1 %Quality	Multivariate	$N=633$ Male: 75% Tetraplegic patients: Age: 40 years old 55% TSI: 10 years ASIA A: 37%	Questionnaire Recurrent PU (at least 1PU/year)	Neurological level Sex Ethnicity Age at onset TSI Personality (Zuckerman Kuhlman personality Questionnaire) Behavioral risk factors[¥] (Behavioral risk factor surveillance system) Protective behavioral factors[¥] (life style questionnaire, detailed but not referenced) Depression (Older adult health and mood inventory)	NS NS NS NS S S: Nervousness-anxiety S: Cigarette smoking, sleeping pills S: Employment, healthy way of life, Regular physical activity, healthy diet. NS: regular self-lifting for weight shifting, skin monitoring…) S
Salzberg[14]	Historical cohort Monocenter, USA Between 1987 and 1993 Quality Assessment: 50%	Multivariate	$N=219$	Clinical or interviews NPUAP scoring system	Gender Professional status Age at injury Age TSI Etiology Neurological level Transversal extension (complete, incomplete) Level of activity (ambulatory, confined in bed, wheelchair use) Mental status Bladder incontinence Bowel incontinence Associated disorders Renal or cardiac diseases, diabetes mellitus, impaired cognitive function, autonomic dysreflexia Pulmonary infection, sepsis Blood analysis Albumin $<34\,g\,dl^{-1}$ Cigarette smoking Alcohol use	NS NS NS NS NS NS NS S S NS S S NS S S S NS

Table 1 Continued

Study	*Design*	*Analysis type*	*Population*	*PU variable*	*Factors studied*	*Results*
Chen[11]	Cohort Multicenter (National Spinal Cord Injury Database, USA) 1973 to 2000 Quality Assessment: 82.1%	Multivariate	$N=3361$ Male: 83% Tetraplegic: 48% ASIA A: 54%	Clinical assessment NPUAP scoring system	Gender Ethnicity Marital status Educational level Professional status Etiology Lesion level Transversal extension (ASIA) PU during acute SCI Medical or surgical associated disorders (4 categories: pulmonary embolism, deep venous thrombosis, pneumonia, kidney stones surgery) Re-hospitalization (regardless of the reason) At home nursing care	S: male (OR = 1.3) S: African-American (OR = 1.7) S: married (OR = 0.7) S: Educational level lower than a University degree (OR = 1.3) S: employee or student (OR = 0.7) NS NS S: ASIA A (OR = 8), B (OR = 6), C (OR = 3) S: OR = 1.4 S: OR = 1.4 S: OR = 1.8 S: OR = 1.6

Abbreviations: ER, Emergency room; NPUAP, National Pressure Ulcer Advisory Panel; NS, non-significant; OR, odds ratio; PU, pressure ulcer; SCI, spinal cord injury; TSI, traumatic spinal cord injury.
[¥]Risk factors with major measurement bias (§) patients with a history of lung disease tend to develop PUs later than those without.
[a]This study is presented as a case control study by the authors, but is in fact a cross sectional design.

Table 2 Socio-demographic and neurological PU risk factors for chronic SCI

	Chen[11]	*Mc Kinley*[13]	*Garber*[12]	*Salzberg*[14]	*Krause 2004*[19]	*Raghavan*[17]	*Krause 98*[20]	*Krause 2001*[18]	*Fuhrer*[4]	*Klotz*[21]	*Anson*[22]	*Risk factor*	*Evidence level*
Quality assessment (%)	82.1	82.1	67.8	50	82.1	82.1	71.4	71.4	67.8	60.7	53.6		
Type of study	Cohort	Cohort	Cohort	Historical cohort	Cross sectional	Cross sectional	Cross sectional	Cross sectional	Cross sectional	Cross sectional	Cross sectional		
Socio-demographic factors													
Gender	Male	Male	—	NS	NS	NS	NS	—	NS	NS	—	Yes	Strong
Age	NS	NS	NS	NS	—	NS	NS	—	NS	NS	—	No	Strong
Ethnicity	Afr	—	NS	—	NS	—	NS	—	NS	—	—	ND	
Educational level	Low	—	NS	—	—	—	—	Low	NS	Low	—	Yes	Moderate
Professional status	Without	—	NS	NS	—	NS	Without	Without	—	Without	—	Yes	Moderate
Marital status	S	—	NS	—	—	NS	—	S	NS		—	Yes	Moderate
Neurological factors													
Age at time of injury	—	—	Young	NS	NS	—	NS	—	—	Young	—	Yes	Moderate
Time since injury	S	S	S	NS	S	—	NS	—	NS	S	S	Yes	Strong
Etiology	NS[a]	Traum	—	NS	—	—	—	—	—	—	—	No	Moderate
Lesion level	NS	NS	—	NS	NS	—	Cervical	—	NS	—	NS	No	Strong
Transversal extension	S	S	—	S	—	—	S	—	NS	S	—	Yes	Strong
Vertical extension	—		S	—	—	—	—	—	S	—	—	Yes	Moderate

Abbreviations: ND, Not determinable; No, not a risk factor; NS, non-significant; PU, pressure ulcer; SCI, spinal cord injury; Yes, risk factor.
[a]After multivariate analysis, taking into account demographic factors.

Table 3 Clinical and functional risk factors during chronic SCI

	Chen[11]	*Mc Kinley*[13]	*Garber*[12]	*Salzberg*[14]	*Niazi*[15]	*Raghavan*[17]	*Fuhrer*[4]	*Klotz*[21]	*Sumiya*[16]	*Risk factor*	*Evidence level*
Quality assessment (%)	82.1	82.1	67.8	50	428	82.1	67.8	60.7	46.4		
Type of study	Cohort	Cohort	Cohort	Historical cohort	Case control	Cross sectional	Cross sectional	Cross sectional	Cross sectional		
Medical factors											
Cardiovascular disease	—	—	—	NS	S	—	—	—	—	ND	
Diabetes mellitus	—	—	—	NS	NS	—	—	—	—	No	Insufficient
LLF	—	S	—	—	—	—	—	—	—	Yes	Moderate
DVT	S	S	—	—	—	—	—	—	—	Yes	Strong
Autonomic dysreflexia	—	S	—	NS	—	—	—		—	Yes	Moderate
Pneumonia	S	S	—	S	—	—	—	—	—	Yes	Strong
Skin-related factor											
PU history	S[a]	—	S	—	—	—	—	S[a]	—	Yes	Strong
PU surgery	—	—	S	—	NS	—	—	—	—	ND[b]	
Biological factor											
Low albumin levels	—	—	—	S	—	—	—	—	—	Yes	Insufficient
Functional factors											
Disability (FIM)	—	—	S	—	—	—	S	—	—	Yes	Moderate
Handicap (Chart)	—	—	S	—	—	—	NS	—	—	Yes	Insufficient
Level of activity	—	—	—	S	S	—	—	—		Yes	Moderate
Bladder incontinence	—	—	—	S	—	NS	—	—	S	Yes	Insufficient
Bowel incontinence	—	—	—	S	—	NS	—	—	—	ND	

Abbreviation: DVT, deep venous thrombosis; LLF, lower limb fracture; ND, Not determinable; No, not a risk factor; NS, non-significant; PU, pressure ulcer; SCI, spinal cord injury; Yes, risk factor.
[a]During acute SCI stage.
[b]Possible confusion bias.

was validated by a cohort study.[12] The level of evidence is moderate.

The mobility level (walking, in a wheelchair or in bed) was evaluated in a case study and a historical cohort study. A low mobility level is a PU risk factor with a moderate level of evidence.

Handicap is a risk factor found in one cohort study.[12] The level of evidence is insufficient.

Bladder or bowel incontinence is also a risk factor suggested in epidemiological studies. Sumiya *et al*. found a causal relationship between bladder incontinence and PU existence in a cross-sectional study.[16] Raghavan *et al*.[17] found no correlation between PU and bladder or bowel incontinence in another cross-sectional study. However, Salzberg *et al*.[14] found a statistical link in a historical cohort study with a low methodological level. Bladder incontinence is a risk factor but there is an insufficient level of evidence.

Factors linked to a medical history of PUs. *History of PU surgical treatment* was reported in two studies and is being identified as a risk factor for recurrent PU.[12,15]

PU medical history[11,12,21] is a risk factor for recurrent PU found in a cross-sectional study[21] and two cohort studies[11,12] (OR: 1.4; 95% CI = 1.2–1.6).

Skin-specific protective behaviors (Table 4). These are the specific prevention techniques taught to SCI patients during their PM&R stay.

A daily skin check-up is found to be a protective behavior in one cross-sectional study,[17] but not in two other cross-sectional studies.[17,19] A cohort study reports a correlation between daily skin monitoring at the time of inclusion and the lack of PU onset up to the third year of follow-up.[12] We can consider skin monitoring as a protective factor with a moderate level of evidence.

The other practices taught to patients such as weight redistribution,[17–19] or regular repositioning in bed,[18,19] are not associated with the lack of a PU. The studies reporting these elements are cross-sectional. For these cross-sectional studies we find a confusion bias for evaluating these factors: some patients who developed a PU at the time of the survey had probably increased their prevention level because of this affection. There is no longitudinal study available for these factors. We cannot determine the importance of these protective factors.

General protective health behaviors. Some general factors, such as daily exercising, healthy diet or a healthy lifestyle were assessed in cross-sectional studies,[18,19] with conflicting results. Thus, they are potentially protective factors with an insufficient level of evidence.

Toxic substances and psychological factors. *Cigarette smoking* is a risk factor identified in three cross-sectional studies[17–19] and confirmed by a historical cohort study.[14] The statistical

Table 4 Behavioral, toxic and psychological risk or protective factors

	Garber[12]	*Salzberg*[14]	*Niazi*[15]	*Raghavan*[17]	*Krause 2004*[19]	*Krause 2001*[18]	*Anderson*[23]	*Sumiya*[16]	*Risk or protective factor*	*Evidence level*
Quality assessment (%)	67.8	50	42.8	82.1	82.1	71.4	46.4	46.4		
Type of study	Cohort	Historical cohort	Case control	Cross sectional	Cross sectional	Cross sectional	Cross sectional	Cross sectional		
Skin-specific protective health behaviors										
General	—	—	—	—	—	—	S[b]	S	Potential	Insufficient
Daily skin monitoring	S	—	—	S[a]	NS[a]	NS[a]	—	—	Yes	Moderate
Turns frequently in bed	—	—	—	—	NS[a]	NS[a]	—	—	ND	
Weigh shifting (self-lifting)	—	—		NS[a]	NS[a]	NS[a]	—	—	ND	
Keep skin dry	—	—	—	—	NS[a]	NS[a]	—	—	ND	
General protective health behaviors										
Regular physical activity	—	—	—	—	S	NS	—	S	Potential	Insufficient
Healthy diet	—	—	—	—	S	NS	—	—	Potential	Insufficient
Healthy lifestyle	—	—	—	—	S	NS	—	—	Potential	Insufficient
Toxic abuse										
Cigarette smoking	—	S	NS[c]	S	S	S	—	—	Yes	Moderate
Alcohol	—	NS	—	—	—	NS	—	—	No	Moderate
Sleeping pills	—	—	—	—	S	—	—	—	Potential	Insufficient
Psychological factors										
Depression	—	—	—	—	S	NS[d]	—	—	Potential	Insufficient
Personality	—	—	—	—	Anxiety	—	—	—	Potential	Insufficient
Self-esteem	—	—	—	—	—	—	NS	—	No	Insufficient

[a]Possible confusion bias.
[b]Evaluated with RESPON questionnaire, not referenced.
[c]$P = 0.057$.
[d]Suicidal behavior.

link tends to be quite significant ($P = 0.057$) in a case–control study.[15] The level of evidence is moderate.

Alcohol abuse is not a PU-related risk factor in a cross-sectional study[18] and a retrospective cohort study. The level of evidence is moderate.

A cross-sectional study[19] reports a link between taking hypnotic drugs and the formation of a PU. It is a potential risk factor with an insufficient level of evidence.

If suicidal behaviors were not related to PU prevalence in a first cross-sectional study,[18] *depression and personality disorders such as anxiety* were linked to PU in a second cross-sectional study.[19] They are potential risk factor with an insufficient level of evidence.

Care-related risk factors. SCI patients being hospitalized for an affection other than PU is also found to be a risk factor, with a moderate level of evidence (OR = 1.8; 95% CI = 1.6–2.2).[11]

Discussion

The objective of this second part of our systematic literature review was to determine the PU risk factors in chronic SCI patients.

Contrary to the risk factors found in the acute stage of SCI patients' care,[9] the risk factors for chronic SCI patients are quite numerous and depend for the major part on the socio-demographic, medical, neurological, cutaneous or behavioral characteristics of the patients.

The results from the epidemiological studies are similar for most of the risk factors found in our review. It is, however, necessary to modulate some of them.

The *African American* origin is reported as a PU risk factor in a US cohort study.[11] The African American SCI subpopulation is very different from the rest of the SCI population at a social level but also at a medical level: violent etiology is more frequent (gunshot wounds), unemployment, lower level of education, difficulty in access to proper healthcare ….[26] This risk factor is most probably correlated to specific US characteristics and should only be carefully extrapolated to other countries.

The results regarding *history of former PU surgery* are apparently conflicting between two studies. A more precise analysis of the studied criteria showed that these results might not be opposed. Niazi *et al*. reported in a case–control study[15] that having a history of PU surgery was not related to PU recurrence at the same location in the long term, suggesting that PU surgery does not weaken the skin tissue in the long-term. Garber *et al*., in a cohort study,[12] highlighted that a history of PU surgery was correlated to PU recurrence without furnishing any details of the precise location of this recurrence (on the surgical site or not). This matches the clinical picture of patients with recurrent PUs.

Medical history of PUs is also a PU risk factor. Cohort studies reporting this correlation do not precisely indicate if it is a

recurrent PU or if the PU originates at another location. In the first case, the time delay up to PU recurrence is interesting to analyze as the remodeling of the scar tissue, at an anatomopathological level, takes about 18 months and this delay is theoretically a period of cutaneous weakness.[27–29] In the second case, this relationship tends to highlight the predisposition of some patients to develop recurrent PUs. The link between PU recurrence and PU surgery must be interpreted with caution. An existing PU—which is a risk factor for recurrence—can already be a potentially confusing factor. Surgical indication and surgical techniques and post-surgical care must also be carefully evaluated before validating them as risk factors.

If, on an anatomopathological risk factor scale, urine and feces toxicity on the skin is quite admitted,[30] the level of evidence for the effect of *bladder/bowel incontinence* at the onset of PU in SCI patients is low.[14,16,17] In comparison, cohort studies conducted in elderly individuals at home show that bladder/bowel incontinence is a risk factor for PU.[31–33] A recent case–control study[34] undermines the effect of urinary incontinence in elderly individuals, by including in the multivariate analysis the individual's degree of independence in daily life activities. Urinary incontinence would only be a confusing factor for other variables related to the loss of independence.

Cigarette smoking is a PU risk factor with a moderate level of evidence. The pathophysiological context of this factor is the effect that smoking has on cutaneous blood flow.[35–38] Viehbeck *et al*.[39] have evaluated the effect of an educational program delivered to SCI patients on the effects of smoking on PU development and scarring. This educational message was delivered through videotape and was memorized in the short term. The effect of this type of prevention on the development of PU onset has not been assessed. *''Protective'' factors* (weight redistributing, self-repositioning, daily skin monitoring, etc.) were assessed in cross-sectional studies thus leading to a bias: it is difficult to know whether this behavior occurs before or after the development of a PU. The level of evidence of these educational practices, taught daily to our patients, is very insufficient.

We were also quite surprised by the low level of evidence and the very few number of studies focusing on the psychological risk factors as these recurrence factors are often encountered in everyday clinical practice.

The analysis of the risk factors for chronic SCI highlights two types of risk factors: on the one hand, the risk factors that are easy to quantify with a level of evidence that is sometimes highly satisfying, such as socio-demographic factors or neurological factors. These factors are hardly affected by prevention. In contrast, there is another category of risk factors with a very low level of evidence and it is hard to quantify it as a behavioral factors category. Behavioral factors can, however, benefit for a primary or secondary prevention strategy: in fact, educational programs for the prevention of PUs development are part of the missions of physical medicine and rehabilitation.[40,41] Furthermore, educational programs or training on PU prevention have a positive effect on the knowledge of the healthcare professionals and thus on PU incidence.[42–45] SCI patients must leave their PM&R center with a good understanding of this pathology and how to prevent the development of PUs as they will be in charge of this prevention at home.

Study limits

Besides the limits listed in the first part of this study,[9] the inclusion of cross-sectional studies in the systematic review was particularly problematic in the second part of our literature review; this study type does not always show a causality relationship, mandatory for validating a risk factor. In fact, the temporal sequence (does the incriminated factor take place before or after the development of the disease?—is not easy to establish. We took this bias into account by grading the causality relationship according to the type of study and its methodological quality.

Perspectives

The evaluation of implementing an *educational workshop* on PU prevention for SCI patients must be based on two aspects: first the beliefs and knowledge of patients both in the short and middle term; and second, the effect in terms of PU incidence in primary or secondary prevention.

Garber *et al*.[46] conducted a pilot study evaluating the effect of a standardized educational program in a low-power, randomized controlled study on a population of SCI patients hospitalized for PU surgery ($N=41$). The effect of the patients' knowledge, assessed by a non-validated questionnaire and the PU recurrence rate are significant for up to 24 months of follow-up. The preliminary results had motivated this team to continue and expand the clinical study with a provisional sample group of 278 patients over a 4-year period[47] to increase the power of the study. The recruiting difficulties and the patients that were unavailable for follow-up did not allow finalization this study. In a second publication on this study, the authors focused on the effect of educational programs on PU recurrence with a positive effect of an individualized educational program with a structured follow-up on the time delay before PU recurrence.[48]

Finally, it is necessary to discuss the efficacy of an educational strategy that would require the creation and validation of an evaluation tool. A scale allowing evaluation of the knowledge of SCI patients on skin risk factors and PU prevention was recently published in the English language.[49–51] This tool could evaluate, in an objective manner, the effect of an educational workshop and also increase the level of evidence of behavioral factors. A validation project in the French language is underway.

Conclusion

The aim of this literature review was to determinate the risk factors for PU development at each stage of SCI patients' care. During acute SCI, the risk factors are essentially related to care modalities, whereas for chronic SCI stage, there are more risk factors: socio-demographic, clinical and

behavioral. The level of evidence of the various factors varies, which could be the focus of additional and complementary studies. The results of this review justify rethinking the organization of care and the management of PU prevention during the various stages of SCI patients' care.

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