



Positive End-Expiratory Pressure in Rhinoplasty Surgery; Risks and Benefits

Ali Faghih Habibi¹ · Ali Ashraf² · Zahra Ghanavi³ · Maryam Shakiba⁴ · Shadman Nemati¹ · Vahid Aghsaghloo¹

Received: 6 February 2023 / Accepted: 2 May 2023
© Association of Otolaryngologists of India 2023

Abstract

Aims The aim of this study is to evaluate the effect of Positive End Expiratory Pressure (PEEP) on surgical field bleeding and its respiratory and hemodynamic consequences in rhinoplasty surgeries.

Materials and methods This single-blind clinical trial performed in Amir Al-Momenin university Hospital in 2018. Seventy cases of rhinoplasty surgery patients Enrolled and were randomized into two groups; intervention (PEEP=5) and comparison group (PEEP=0). Surgical field bleeding and arterial oxygen saturation pulmonary dynamics and hemodynamic parameters were evaluated during operation and in post anesthesia care unit. Data were analyzed by SPSS software using descriptive and analytical statistics.

Results PEEP applying had no negative effect on surgical bleeding as well as surgeon satisfaction, heart rate and blood pressure were similar in two groups. Pulmonary dynamics and oxygenation were stable and within normal values in all cases. The mean peak airway pressure was 17.87 ± 2.24 in the PEEP group and 16.08 ± 3.37 in the ZEEP group ($P=0.029$).

Conclusion applying low level PEEP during anesthesia improved recovery oxygen saturation but had no negative effects on the patient's hemodynamics, and did not aggravate bleeding and visual clarity.

Keywords Anesthesia · PEEP · Rhinoplasty · Rhinoplasty Surgery

Introduction

Rhinoplasty is a common operation as a cosmetic surgery. According to the researches in Iran, 180 out of every 100,000 population underwent rhinoplasty surgery per year, which is considered to be one of the highest rates of rhinoplasty in the world [1, 2]. Rhinoplasty is performed in a narrow space area at the proximity of vital and delicate

tissues as orbits and sinuses and skull base, thus bleeding during surgery that reduces the surgeon's sight of view, can cause surgical complication [3]. Surgical field bleeding can lead to unwanted events and increase the risks of surgical complications such as prolonged anesthesia and surgery and needs to be managed, it can increase surgical stress for the patient and can annoys surgeon and anesthesiologist [4]. Reducing bleeding can make surgery easier and can lead

✉ Ali Ashraf
ashraf_adr@yahoo.com

Ali Faghih Habibi
dr.faghih.habibi@gmail.com

Zahra Ghanavi
dr.z.ghanavi@gmail.com

Maryam Shakiba
shakiba_mm@yahoo.com

Shadman Nemati
drshadmannemati_ent@yahoo.com

Vahid Aghsaghloo
dr.vahiiiiid@gmail.com

¹ Otorhinolaryngology Research Center, Department of Otolaryngology and Head and Neck Surgery, School of Medicine, Amiralmomenin Hospital, Guilan University of Medical Sciences, Rasht, Iran

² Clinical Research Development Unit of Poursina Hospital, Guilan University of Medical Sciences, Rasht, Iran

³ Department of Neurosurgery, School of Advanced Medical Sciences and Technologies, Shiraz University of Medical Sciences, Shiraz, Iran

⁴ Department of Biostatistics & Epidemiology, School of Health, Guilan University of Medical Sciences, Rasht, Iran

to positive surgical progression in these conditions. Nasal mucosa is enriched of blood vessels and blood flow. This rich blood flow provides heat and humidifies the inhaled air. Therefore, spontaneous or traumatic bleeding can happen in this area. The existence of a common capillary network and rich blood flow causes excessive bleeding during surgery [5]. The benefits of a clean and blood-free surgery field on the outcomes of these patients are widely accepted by surgeons and anesthesiologists as well as patients [6, 7]. Different technics as patient's head elevation and position, deliberate hypotension or antithrombotic medications like tranexamic acid has been recommended and used for this reason [3]. The use of positive end-expiratory pressure has become common due to its beneficial respiratory effects in the postoperative phase, especially in prolonged operation and obese patient's surgery and patients undergoing laparoscopy [8, 9]. However, PEEP may increase intrathoracic pressure and thus reduce venous return. Some authors have suggested that venous congestion of the head and neck may cause poor surgical vision due to increased bleeding, but that lowering blood pressure following PEEP may also compensate the earlier effect of peep [10, 11]. Several studies have been performed to determine the ideal amount of PEEP so as not to disturb hemodynamics and to improve oxygen delivery [12, 13]. The application of different levels of PEEP has been suggested to treat atelectasis and improve arterial oxygenation status [14, 15]. According to the high prevalence of rhinoplasty in Iran and especially in Guilan province, also the lack of similar studies on the effect of peep in these surgeries [16, 17], we decided to investigate the effect of positive end expiratory pressure on respiratory and hemodynamic parameters and intraoperative bleeding in Rhinoplasty patients referred to Amir Al-Momenin Hospital in 2019.

Methods

This study is a single-blind randomized clinical trial performed in Amir Al-Momenin university hospital from 2018 to 2019, patients aged 18 to 40 years referred for rhinoplasty enrolled in this study. Ethical approval for the study was obtained by the Local Research Ethics Committee of Guilan University of Medical Sciences and the study adhered to the tenets of the World Medical Association Declaration of Helsinki (REC.1396.400). After obtaining written informed consent, patients were randomly divided into two groups of 34 using a random generator program. In the PEEP (group A), positive expiratory end pressure of 5 cm of H₂O was applied and ZEEP (group B) underwent ventilation during rhinoplasty without applying PEEP. Age gender weight and height as demographic data were recorded and hemodynamic

condition as systolic and diastolic blood pressure heart rate and arterial oxygen saturation were monitored during anesthesia an in-recovery hall in 30 min intervals.

Patients with a history of anticoagulants, aspirin or NSAID and opioid drugs abuse and addiction, or underlying lung disease were excluded. The study conditions were explained to the patients by the relevant physician and informed consent was obtained for participating in the study. Patients were randomly divided into two groups of intervention and comparison by random sequencing. The random ratio was 1: 1 and a random sequence was prepared from the Random generator program. Patients were assigned based on sequences determined by the anesthesia nurse. 5 cm of water peep was applied for the intervention group (group A) and no PEEP (0 cm H₂O) was used in the comparison group (group B) All patients underwent surgery and anesthesia using (Drager Fabius plus anesthesia machine, Germany) with airway pressure monitoring. All hemodynamic and respiratory parameters and oxygen saturation were recorded as zero study time before the intervention. After prescribing Midazolam 1–2 milligram as premedication, Pre-oxygenation, Fentanyl 1.5–2 micg/kg as analgesic medication injected, anesthesia induced by injection of 0.2 mg/kg cisatracurium and 1.5 mg/kg Propofol. Tracheal Intubation was done 3–4 min later under view of direct laryngoscopy Macintosh blade. mechanical ventilation with a 8ml / kg tidal volume and respiratory rate of 10–12 b/m for the group B as intervention 5 cm of H₂O applied in form of PEEP. Anesthesia and operation were conducted with Total intravenous anesthesia (TIVA) method by infusion of propofol remifentanyl to achieving BIS (bispectral Index) between 40 and 60. The amount of suctioned blood from fields of surgery as milliliter and surgeon satisfaction from field as the Boezaart index were recorded and compared in two groups. At the end of operation, reversal of the muscle relaxants confirmed with the train of four and double burst index. After extubation patient transferred to the post anesthesia care unit (recovery). The changes of each characteristic were measured and finally, the two groups were compared in terms of variables.

Statistical Analysis

The obtained data were analyzed by SPSS 22 software using descriptive and analytical statistical tests. Data normality was measured by the KS test. Chi-square and t-test were used to compare the underlying variables and covariance analysis and the GEE test was used to compare the changes in blood and respiratory indices between the two groups at different times and measure values before the intervention. The significance level was considered below 0.05. Sample size based on the results of a pilot study on 16 patients and

Table 1 Preoperative Data

Variable	group	PEEP group (n=34)	ZEEP group (n=34)	P value
Gender	Man	1(2.9)	1(2.9)	0.1
	Female	33(97.1)	33(97.1)	
Mean age (year)	Less than 20	8(22.5)	7(20.6)	0.415
	20–30	18(52.9)	14(41.2)	
Mean BMI	More than 30	8(23.5)	13(38.2)	0.282
	Less than 19	3(8.8)	4(11.8)	
	19–25	22(64.7)	16(47.1)	
	25–30	8(23.5)	9(26.5)	
	More than 30	1(2.9)	5(14.7)	

BMI: body mass index, PEEP: positive end-expiratory pressure, ZEEP: zero added PEEP.

Table 2 Surgical Field in Functional

	group	Mean ± SD	P-value
Peak airway Pressure	PEEP	17.87 ± 3.24	0.029
	ZEEP	16.08 ± 3.37	
Plateau airway Pressure	PEEP	14.74 ± 2.79	0.086
	ZEEP	13.56 ± 2.82	
Tidal Volume	PEEP	547 ± 89.28	0.675
	ZEEP	556.5 ± 97.07	
ET CO2	PEEP	28.41 ± 1.43	0.0001
	ZEEP	29.71 ± 1.11	
During surgery	PEEP	99.21 ± 0.62	0.639
	ZEEP	98.13 ± 0.72	
Recovery time	PEEP	98.02 ± 1.36	0.79
	ZEEP	98.1 ± 1.2	

PEEP: positive end-expiratory pressure, ZEEP: zero added PEEP, ET/CO2: End-tidal CO2 (mm Hg)

estimating the following indicators in the rate of bleeding between the two pilot groups, and considering the 90% power and 95% confidence level and 20% of the sample loss using the conventional sample volume formula compared Two averages of 34 people in each group were calculated.

Results

The mean age of the PEEP group was 26.0 ± 6.74 years and the ZEEP group was 27.05 ± 6.85 years. 66 (97.1%) of the total sample were female, and 2 (2.9%) were male. A Chi-square test was used to evaluate the homogeneity of groups in terms of demographic variables. The results showed that there was no statistically significant relationship between the frequency distribution of gender (P=0.1), age groups (P=0.415), and BMI categories (P=0.282) in rhinoplasty. Also, using the t-test, it was found that there was no statistically significant difference between the mean age of the two groups (P=0.523) (Table 1).

Table 3 Quality of Surgical Field (Boezaart Grading System)

Grade	Assessment of surgical field	PEEP	ZEEP	P-value
0	No bleeding.	5(14.7)	0(0)	0.163
1	Slight bleeding—no suctioning required.	11(32.4)	10(29.4)	
2	Slight bleeding, occasional suctioning required. The surgical field is not threatened.	8(23.5)	11(32.4)	0.163
3	Slight bleeding—frequent suctioning required. Bleeding threatens surgical field a few seconds after suction is removed.	8(23.5)	11(32.4)	
4	Moderate bleeding—frequent suctioning required. Bleeding Threatens the surgical field directly after suction is removed.	2(5.9)	1(2.9)	0.163
5	Severe bleeding—constant suctioning required. The bleeding appears faster than can be removed by suction. The surgical field is severely threatened and surgery not possible.	0(0)	1(2.9)	

The mean values of (Plateau airway Pressure) (cm of water) were higher in PEEP group but the difference was not statistically significant (P=0.86).

Mann-Whitney and t-test showed that mean values of maximum airway pressure (cm H2o) had significantly statistical different (P=0.029) in two groups rhinoplasty patients with PEEP and ZEEP. There was no statistically significant difference between; ventilation tidal volume, CO2 pressure in exhaled air (End-tidal CO2), Boezaart index values and surgical field bleeding (ml) between case and control groups (Table 2), (Table 3). Using Fisher’s generalized test, it was found that there was no statistically significant relationship between the frequency distribution of the Boezaart index score between two groups (P=0.163) (Table 3). By using of independent t-test and Mann-Whitney tests, it was found that there was no statistically significant difference between the mean percentage of arterial blood oxygen saturation (O2-Saturation) during surgery (P=0.916) and recovery (P=0.79), in two groups. Also, there was no statistically significant difference between the mean systolic blood pressure (mmHg) during surgery (P=0.616) and recovery (P=0.529) in two groups and also between the mean diastolic blood pressure (mmHg). A significant association between surgery (P=0.604) and recovery time (P=0.432) and the mean heart beats rate per minute during surgery (P=0.88) and recovery time (P=0.096) in the two groups was not observed (Table 4). Using the chi-square test, found that needs for antihypertensive drugs for deliberate hypotension and blood

Table 4 Intraoperative Data

	Timeline	group	Mean \pm SD	P-value	
O ₂ -Saturation	During surgery	PEEP	99.21 \pm 0.62	0.639	
		ZEEP	98.13 \pm 0.72		
	Recovery time	PEEP	98.02 \pm 1.36		0.79
		ZEEP	98.1 \pm 1.2		
Systolic blood pressure (mm Hg)	During surgery	PEEP	100.85 \pm 6.4	0.616	
		ZEEP	101.85 \pm 9.65		
	Recovery time	PEEP	119.7 \pm 16.31		0.529
		ZEEP	121.95 \pm 12.74		
Diastolic blood pressure (mm Hg)	During surgery	PEEP	62.96 \pm 8.28	0.604	
		ZEEP	64.05 \pm 8.93		
	Recovery time	PEEP	78.28 \pm 11.81		0.809
		ZEEP	79.01 \pm 12.83		
Heart rate (bpm)	During surgery	PEEP	81.3 \pm 6.65	0.88	
		ZEEP	80.97 \pm 10.73		
	Recovery time	PEEP	83.88 \pm 11.26		0.096
		ZEEP	79.12 \pm 11.99		

PEEP = positive end-expiratory pressure; ZEEP = zero added PEEP.

Table 5 Frequency distribution of the need for the antihypertensive drug during surgery in two groups

Period time	Group Need to inject the antihypertensive drug	PEEP	ZEEP	P-value
Start surgery	YES	3(8.8)	5(14.7)	P=0.709
	NO	31(91.2)	29(85.3)	
15 min	YES	9(26.5)	6(17.6)	P=0.38
	NO	25(73.5)	28(82.4)	
30 min	YES	9(26.5)	7(20.6)	P=0.709
	NO	25(73.5)	27(79.4)	
45 min	YES	3(8.8)	2(5.9)	P=0.64
	NO	31(91.2)	32(94.1)	
60 min	YES	1(2.9)	0(0)	P=0.314
	NO	33(97.1)	34(100)	
75 min	YES	0(0)	0(0)	...
	NO	34(100)	34(100)	

pressure control during surgery was not statistically significant between the groups ($P=0.215$). According to the results of the chi-square test and Fisher's exact test, it was found that there is no statistically significant relationship between the need for an injection of an antihypertensive drug from the time of surgery to 75 min (during surgery) in both groups ($P<0.05$). Also, at 75 min after surgery, none of the patients in two groups studied needed antihypertensive drugs. (Table 5)

The amount of bleeding was measured by recording the amount of suctioned blood during the operation and calculating its difference with the amount of serum used for washing. Surprisingly intraoperative bleeding was lower in the PEEP group (71.61 ± 46.65) and in the non-application group was 108.23 ± 101.52 although Mann-Whitney U test showed that bleeding rate (ml) two groups of PEEP and

ZEEP have not statistically significant difference but applying positive end-expiratory pressure ($P=0.06$).

Discussion

During general anesthesia diaphragm and respiratory muscles are paralyzed and oxygenation and safety of anesthesia depends on how much alveolar recruitment is preserved and recovered after that in post anesthesia period. Applying PEEP can theoretically improve respiratory parameters although at the same time can reduce cardiac output and stimulate cardio accelerator fibers to compensate the hemodynamic and cardiac output changes. These make anesthesiologist to hesitate using peep as a protective strategy. At the same time peep can reduce right heart blood return and head and neck vessels engorgement that increase risk of bleeding in surgeries in these areas. Based on the results of this study PEEP application even in a short period of time (during surgery) improved oxygenation indices in patients under ventilation and also during post anesthesia care. As in similar studies, no statistically significant differences were observed between two groups in any of the demographic indicators [18, 19]. Local bleeding in rhinoplasty is difficult to control due to the anatomical and pathological features of that area [18]. In our study applying PEEP not only interfered bleeding or surgical field blood loss but also these were not significantly lower in this group of rhinoplasty surgery that it can be due to hemodynamic and cardiac output effect of PEEP, the same as another study in hepatic surgery in 2016, that showed volume of blood lost in the PEEP group was 275 cc and in the group without PEEP 500 cc, which according to our study, no negative effect and exaggerated bleeding observed [20]. In this study, the mean systolic and diastolic blood pressure of patients during surgery was 100- and 62-mm Hg and 101- and 78-mm Hg in PEEP and ZEEP group, respectively, but no significant relationship was observed between PEEP use and pressure changes in patients. The mean postoperative blood pressure of patients in both groups was higher than intraoperative pressure. Post operative pressure was higher in PEEP than ZEEP group but not significantly. Similar results were obtained in other studies [18, 21, 22]. The mean heart rate of patients during surgery was almost equal in two group's comparison and there was no evidence of unfavorable effect of PEEP on patient's heart rate. The results of other studies also showed that patient's heart rate during surgery was not affected by PEEP [23, 24]. The mean oxygen saturation in two groups of PEEPS and ZEEP was almost equal (99% during surgery and 98% during recovery). Other studies had similar results as ours [18, 19]. In our study, the mean maximal airway pressure (Peak airway pressure) in PEEP group

was 24.3 ± 87.17 and in ZEEP group was 37.3 ± 08.16 . This difference was significant between the groups ($P=0.029$). In this study, as in another similar study, plateau airway pressure was higher in group PEEP than in group ZEEP [19, 25], but no significant statistical difference was observed between two groups. In PEEP group, the mean ventilation tidal volume was 547 ± 89.28 ml and in ZEEP group, this was 556.5 ± 97.07 ml and no statistically significant difference was observed between the two groups ($P=0.675$).

Conclusion

In general, it can be concluded that in this study, PEEP applying does not have negative prominent hemodynamics effect and the surgeon's visual acuity was not disturbed. PEEP not only not increased blood loss but also controlled better its severity may be by cardiac output effects. PEEP had a positive role in improving intraoperative and postanesthesia arterial oxygenation saturation. So in at risk patients who oxygenation is a critical subject PEEP during surgery, can be considered to reduce the incidence or severity of complications and to respiratory complications.

Authors suggestion is to study PEEP in special conditions and also population like different body mass indexes or respiratory parameters to be able taking right decision in positive pressure ventilation during surgery and prevent unwanted pulmonary complications due to mechanical ventilation.

Supplementary Information The online version contains supplementary material available at <https://doi.org/10.1007/s12070-023-03854-7>.

Acknowledgements We are especially grateful to all the experts who were an integral partner in the preparation of facilities.

Funding None.

Declarations

Conflict of interest The authors declare that they have no conflict of interest.

References

- Ebrahimi A, Kalantar Motamedi MH, Shams A, Nejadsharvari N (2016) Health and social problems of rhinoplasty in Iran. *World J Plast Surg* 5(1):75–76
- Rastmanesh R, Gluck ME, Shadman Z (2009) Comparison of body dissatisfaction and cosmetic rhinoplasty with levels of veil practicing in Islamic women. *Int J Eat Disord* 42(4):339–345
- Ozkose M, Baykan H, Coşkuner İ (2016) The effect of patient positioning on amount of intraoperative bleeding in rhinoplasty: a randomized controlled trial. *Aesthetic Plast Surg* 40(4):453–457
- Flint PW, Haughey BH, Robbins KT, Thomas JR, Niparko JK, Lund VJ et al (2014) Cummings otolaryngology-head and neck surgery e-book. Elsevier Health Sciences
- Nikoyan L, Matthews S (2012) Epistaxis and hemostatic devices. *Oral and Maxillofacial Surgery Clinics* 24(2):219–228
- Sieskiewicz A, Olszewska E, Rogowski M, Grycz E (2006) Preoperative corticosteroid oral therapy and intraoperative bleeding during functional endoscopic sinus surgery in patients with severe nasal polyposis: a preliminary investigation. *Annals of Otolology, Rhinology & Laryngology.* ;115(7):490–4
- Tirelli G, Bigarini S, Russolo M, Lucangelo U, Gullo A (2004) Total intravenous anaesthesia in endoscopic sinus-nasal surgery. *Acta Otorhinolaryngol Ital* 24:137–144
- Futier E, Constantin J-M, Paugam-Burtz C, Pascal J, Eurin M, Neuschwander A et al (2013) A trial of intraoperative low-tidal-volume ventilation in abdominal surgery. *N Engl J Med* 369(5):428–437
- Karsten J, Heinze H, Meier T (2014) Impact of PEEP during laparoscopic surgery on early postoperative ventilation distribution visualized by electrical impedance tomography. *Minerva Anesthesiol* 80(2):158
- Bajwa SJS, Kaur J, Kulshrestha A, Haldar R, Sethi R, Singh A (2016) Nitroglycerine, esmolol and dexmedetomidine for induced hypotension during functional endoscopic sinus surgery: a comparative evaluation. *J Anaesthesiol Clin Pharmacol* 32(2):192
- Webster AC, Morley-Forster PK, Janzen V, Watson J, Dain SL, Taves D et al (1999) Anesthesia for intranasal surgery: a comparison between tracheal intubation and the flexible reinforced laryngeal mask airway. *Anesth Analgesia* 88(2):421–425
- Hall RI, Smith MS, Ricker G (1997) The systemic inflammatory response to cardiopulmonary bypass: pathophysiological, therapeutic, and pharmacological considerations. *Anesth Analgesia* 85(4):766–782
- Dorinsky PM, Whitcomb ME (1983) The effect of PEEP on cardiac output. *Chest* 84(2):210–216
- Tusman G, Böhm S, de Anda GV, Do Campo J, Lachmann B (1999) Alveolar recruitment strategy improves arterial oxygenation during general anaesthesia. *Br J Anaesth* 82(1):8–13
- Auler J Jr, Carmona M, Barbas C, Saldiva P, Malbouisson L (2000) The effects of positive end-expiratory pressure on respiratory system mechanics and hemodynamics in postoperative cardiac surgery patients. *Braz J Med Biol Res* 33(1):31–42
- Niazi M, POURMIRZA KR (2003) The effect of positive end expiratory pressure on incidence rate of atelectasis after coronary artery bypass graft.
- Golparvar M, Abbasi S, Jazi SK (2013) The Effects of different levels of positive end-expiratory pressure on hemodynamic and respiratory indexes in patients with healthy and damaged lungs. *Journal of Isfahan Medical School.* ; 31(239)
- DeMaria S, Govindaraj S, Huang A, Hyman J, McCormick P, Lin HM et al (2015) The influence of positive end-expiratory pressure on surgical field conditions during functional endoscopic sinus surgery. *Anesth Analgesia* 120(2):305–310
- Güldner A, Kiss T, Neto AS, Hemmes SN, Canet J, Spieth PM et al (2015) Intraoperative protective mechanical ventilation for prevention of postoperative pulmonary complications: a comprehensive review of the role of tidal volume, positive end-expiratory pressure, and lung recruitment maneuvers. *J Am Soc Anesthesiologists* 123(3):692–713
- Neuschwander A, Futier E, Jaber S, Pereira B, Eurin M, Marret E et al (2016) The effects of intraoperative lung protective ventilation with positive end-expiratory pressure on blood loss during hepatic resection surgery: a secondary analysis of data from a published randomised control trial (IMPROVE). *Eur J Anaesthesiol (EJA)* 33(4):292–298

21. Ingaramo OA, Ngo T, Khemani RG, Newth CJ (2014) Impact of positive end-expiratory pressure on cardiac index measured by ultrasound cardiac output monitor. *Pediatr Crit Care Medicine| Soc Crit Care Med* 15(1):15–20
22. Sarge T, Loring SH, Yitsak-Sade M, Malhotra A, Novack V, Talmor D (2014) Raising positive end-expiratory pressures in ARDS to achieve a positive transpulmonary pressure does not cause hemodynamic compromise. *Intensive Care Med* 40(1):126–128
23. D'Antini D, Huhle R, Herrmann J, Sulemanji DS, Oto J, Raimondo P et al (2018) Respiratory system mechanics during low versus high positive end-expiratory pressure in open abdominal surgery: a substudy of PROVHILO randomized controlled trial. *Anesth Analg* 126(1):143
24. Kwak HJ, Park SK, Lee KC, Lee DC, Kim JY (2013) High positive end-expiratory pressure preserves cerebral oxygen saturation during laparoscopic cholecystectomy under propofol anesthesia. *Surg Endosc* 27(2):415–420
25. Neto AS, Rabello Filho R, Cherpanath T, Determann R, Dongel-mans DA, Paulus F et al (2016) Associations between positive end-expiratory pressure and outcome of patients without ARDS at onset of ventilation: a systematic review and meta-analysis of randomized controlled trials. *Ann Intensiv Care* 6(1):109

Publisher's Note Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.

Springer Nature or its licensor (e.g. a society or other partner) holds exclusive rights to this article under a publishing agreement with the author(s) or other rightsholder(s); author self-archiving of the accepted manuscript version of this article is solely governed by the terms of such publishing agreement and applicable law.