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Reverse blood flow in cervicofacial veins after venous ligations. Potential implications in microsurgery.

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ABSTRACT :

Introduction : The consequences on the cervico-facial venous circulation of major cervico-facial vein ligations are poorly known. We aimed to highlight by Doppler-Ultrasound flow differences in the cervicofacial venous network in case of unilateral or bilateral ligation of main venous collector trunks (external jugular vein [EJV], internal jugular vein [IJV])

Methods : A Doppler-ultrasound was performed on 10 healthy volunteers, 8 patients with previous bilateral ligation of the external jugular vein (EJV) , 8 with an unilateral ligation of the EJV, and 8 with an unilateral ligation of the EJV and internal jugular vein (IJV) , after modified radical neck dissection. The diameter, the flow direction and the peak systolic velocity (PSV) of the superficial temporal vein, the facial vein and the IJV were measured.

Results : Healthy patients had a similar right and left PSV for all the veins studied, with always antegrade flows. Patients with previous ligations had some significant right/left differences, and retrograde flows.

Conclusion : A redistribution of venous blood flow on the contralateral side of the face and neck seems to take place in case of unilateral ligation of the EJV and/or IJV. Retrograde flows are sometimes observed in case of previous ligation of the EJV and/or IJV, and might compromise the success of venous microanatomoses.

KEYWORDS : Doppler-Ultrasound, vein, blood flow, microsurgery, head and neck.

INTRODUCTION :

Head and neck squamous cell carcinoma (HNSCC) is the sixth most common type of cancer worldwide, tobacco and alcohol representing its most frequent risk factors¹.

Recurrences and second primary cancers remain frequent, occurring usually within 2 years after the initial diagnosis¹. Whether surgery is the primary treatment, or in case of suspected residual disease after treatment with primary chemoradiotherapy², a neck dissection is usually performed.

Although conservative selective neck dissection procedures are nowadays the rule, the surgeon is often brought to ligate main venous collector trunks for carcinologic reasons³. This may result in a redirection of cerebrovenous blood to collateral pathways^{4,5}. However, if blood flow velocity seems to be increased in the contralateral internal jugular vein in case of radical neck dissection⁴, the resulting variations of venous blood flow in the superficial and deep facial venous system remain unknown⁶.

Head and neck defects following large oncologic resections often require microvascular free flaps for head and neck reconstruction⁷. However, iterative ablative surgeries due to tumour recurrence or second primary HNSCC can lead to a lack of adequate recipient vessels⁸. Yet, in microvascular reconstructive surgery the recipient vessels patency is key to a successful outcome⁷. A “ vessel-depleted neck” as well as undetermined venous collateral pathways and unknown hemodynamic effects, can therefore compromise the achievement and the success of microvascular anastomosis^{8,9,10}.

Venous thrombosis being the main cause of free flap failure¹¹, choosing the best recipient vein is essential. Owing to the paucity of data on the head and neck venous network in the literature, we aimed to highlight by Doppler-Ultrasound flow differences in the cervicofacial venous network in case of unilateral or bilateral ligation of main venous

collector trunks (external jugular vein [EJV], internal jugular vein [IJV]). We focused on the superficial temporal vein (STV), the facial vein (FV) and the IJV.

MATERIALS AND METHODS:

The study was conducted between July 2017 and January 2020. It satisfied the European Rules for data protection (General Data Protection Regulation registration number : R201-004-017) of the Regional Comprehensive Cancer Center Léon Bérard (CLB), Lyon, France, and was approved by local Ethics Committee

Twenty-four patients who had previously undergone a neck dissection with ligation of the external jugular vein (EJV) and/or internal jugular vein (IJV) for a HNSCC, and were candidates for a free flap reconstruction requiring a vascular evaluation by Doppler-ultrasound prior to their surgery were included. All patients were operated by the same team of head and neck surgeons, the EJV being systematically ligated at the base of the neck when performing the cervicotomy. The facial vein was preserved whenever possible.

Besides, ten healthy volunteers were recruited among the members of the medical and paramedical staff. Healthy volunteers and patients characteristics are presented in Table 1.A and 1.B. All subjects signed an informed consent form at the time of inclusion.

The 10 healthy volunteers (Healthy volunteers group) served to evaluate the physiological variations of venous blood flow in the superficial veins of the face. They had no history of facial trauma, or head and neck surgery.

The 24 patients who underwent a neck dissection were assigned to 3 groups according to the vein ligated on the operative report:

- Group Bext (n = 8): bilateral ligation of the EJV.
- Group Uext (n = 8): unilateral ligation of the EJV.
- Group Uext + Uint (n = 8): neck dissection with ligation of the EJV and IJV.

A cervico-facial Doppler-ultrasound was performed on all subjects by an experienced vascular physician, using high-frequency, 12-16 Mhz, Affinity 70 G Philips©, pulsed and color Doppler-ultrasound (Figure 1). Doppler-ultrasound was carried out in a head straight and in supine body position during normal breathing. For a matter of reproducibility, all the exams were performed by the same physician.

The mean time between EJV and/or IJV ligation and Doppler-ultrasound examination was 3 [range: 0,7 – 6,6] year for patients of group Bext, 3,3 [range: 0,7 – 12,5] years for patients of group Uext, and 3,3 [range: 0,7 – 11,5] years for patients of group Uext + Uint.

The studied veins were:

- The superficial temporal vein (STV) in the pre-auricular region,
- The facial vein (FV) at the mandibular notch,
- And the internal jugular vein at the base of the neck (IJV) when not ligated.

The measured parameters were:

- The maximum diameter of the vein,
- The flow direction:
 - o Antegrade: venous blood flow moving away from the head towards the heart.
 - o Retrograde: venous blood flow moving away from the heart towards the head.
- And the peak systolic velocity (PSV).

Descriptive statistics were produced using Excel® (Microsofyt corp, USA), and PRISM® (graphpad) software, using Student's paired t test for count data, the patient being his own control.

RESULTS :

1. Superficial temporal vein :

1.1 Healthy volunteers group:

The median diameters of the right and left STV were respectively 1,4 mm and 1,2 mm. The venous blood flow had an antegrade direction on both sides, with a median PSV of 15,4 cm/s for the right STV and 14,5 cm/s for the left STV (Table 2.A).

1.2 Bilateral ligation of the EJV (Group Bext):

The results for the STV of one patient of group Bext were excluded from the analysis, as we were unable to identify its right STV by Doppler-ultrasound. For the remaining patients, the median diameters of the right and left STV were respectively 1,5 mm and 1,4 mm. The venous blood flow had an antegrade direction on both sides, with a median PSV of 19,9 cm/s for the right STV and 9,5 cm/s for the left STV (Table 2.A).

1.3 Unilateral ligation of the EJV (Group Uext):

The median diameter of the STV was 1,8 mm on the ipsilateral side of the EJV ligation and 1,5 mm on the contralateral side. The venous blood flow had an antegrade direction on both sides, with a median PSV of 12,4 cm/s on the ipsilateral side of the EJV ligation, and 25,4 cm/s on the contralateral side. The PSV was significantly decreased on the ipsilateral side of the ligation according to Student's paired t test ($p= 0,014$). It is to note that the PSV was below 5 cm/s for one patient on the ipsilateral side of the EJV ligation (Table 2.A).

1.4 Ligation of the EJV and IJV (Group Uext + Uint):

The median diameter of the STV was 1,2 mm on the ipsilateral side of the EJV and IJV ligation, and 1,3 mm on the contralateral side. Frequent differences were observed between the ipsilateral and contralateral side of the EJV and IJV ligations (Student's paired t test, $p = 0,037$). The venous blood flow had always an antegrade direction on the ipsilateral side of the EJV and IJV ligation, whereas on the contralateral side, one retrograde flow was observed. The median PSV was 6,5 cm/s on the ipsilateral side of the EJV and IJV ligation, and 27,3 cm/s on the contralateral side. The PSV was significantly decreased on the ipsilateral side of the ligation according to student's paired t test ($p=0,017$). It is noteworthy that the PSV was below 5 cm/s for 4 of the 8 patients on the ipsilateral side of the EJV and IJV ligation (Table 2.A).

2. Facial vein :

2.1 Healthy volunteers group:

The median diameters of the right and left FV were respectively 1,4 mm and 1,5 mm. The venous blood flow in the left FV had always an antegrade direction. The median PSV was 30,9 cm/s in the right FV, and 23,5 cm/s in the left FV (Table 2.B).

2.2 Bilateral ligation of the EJV (Group Bext):

The results for the FV of 4 patients of group Bext were excluded from the analysis, as they had one or both facial vein(s) ligated. Otherwise, the median diameters of the right and left FV in this group were respectively 1,7 mm and 1,4 mm. The venous blood flow in the

right and left FV had mostly an antegrade direction, except for 2 patients with one retrograde flow observed in the left FV, and one retrograde flow observed in the right FV. The median PSV was 23,1 cm/s in the right FV and 25,9 cm/s in the left FV (Table 2.B).

2.3 Unilateral ligation of the EJV (Group Uext):

The results for the FV of 1 patient of group Uext were excluded from the analysis, as its facial vein was ligated on the ipsilateral side of the neck dissection. The median diameter of the FV was 2,3 mm on the ipsilateral side of the EJV ligation, and 3 mm on the contralateral side. The venous blood flow had an antegrade direction on both sides, with a median PSV of 20 cm/s on the ipsilateral side of the EJV ligation, and 42,7 cm/s on the contralateral side of the EJV ligation (Table 2.B).

2.4 Ligation of the EJV and IJV (Group Uext + Uint):

The results for the FV of 4 patients of group Uext + Uint were excluded from the analysis, as they had one or both facial vein(s) ligated. The median diameter of the FV in this group when present was 1,9 mm on the ipsilateral side of the EJV and IJV ligation, and 2 mm on the contralateral side of the EJV and IJV ligation. The venous blood flow on both sides had mostly an antegrade direction, however, a retrograde flow was observed for 1 patient on the contralateral side of the ligation. The median PSV was 13,5 cm/s on the ipsilateral side of the EJV and IJV ligation, and 24,9 cm/s on the contralateral side (Table 2.B).

3. Internal jugular vein :

3.1 Control group:

The median diameters of the right and left IJV were respectively 13,5 mm and 11,1 mm. The venous blood flow had an antegrade direction on both sides, with a median PSV of 37,9 cm/s on the right IJV, and 43,2 cm/s on the left IJV (Table 2.C).

3.2 Bilateral ligation of the EJV (Group Bext):

The median diameters of the right and left IJV were respectively 10 mm and 9 mm. There were frequent variations between the left and right side of the neck (Student's paired t test, $p = 0,018$). The venous blood flow had always an antegrade direction in the right IJV, whereas a bilateral flow (antegrade during the systole, and retrograde during the diastole) was observed for one patient in the left IJV. No compression or thrombus of the brachiocephalic vein was found for that patient. His clinical examination was normal, and he didn't have a central venous catheter. The median PSV was 50 cm/s in the right IJV, and 25 cm/s in the left IJV (Student's paired t test, $p = 0,047$)(Table 2.C).

3.3 Unilateral ligation of the EJV (Group Uext):

The median diameter of the IJV was 8,6 mm on the ipsilateral side of the EJV ligation, and 10 mm on the contralateral side of the EJV ligation. The venous blood flow always had an antegrade direction on both sides. The median PSV was 31 cm/s on the ipsilateral side of the EJV ligation, and 50,7 cm/s on the contralateral side of the EJV ligation (Table 2.C). The

PSV was significantly decreased on the ipsilateral side of the ligation according to student's paired t test ($p = 0,031$).

3.4 Ligation of the EJV and IJV (Group Uext + Uint):

The median diameter of the IJV on the contralateral side of the EJV and IJV ligation was 11,6 mm. The venous blood flow had always an antegrade direction, with a median PSV of 33 cm/s (Table 2.C).

DISCUSSION :

There is so far no gold standard as for how to explore the cervico-facial venous system. We chose Doppler-Ultrasound as it is a noninvasive, readily available, reproducible and cost-effective technique for the examination of cervico-facial veins¹². We chose to study the STV, the FV, and the IJV because these vessels are easy to explore by Doppler-Ultrasound^{13,14}, and frequently used as recipient vessels in microsurgical reconstruction of the head and neck⁷. They are also often the only recipient veins left after iterative surgeries or radical neck dissection^{8,9,10}. Analogously to the quality standards of arterial Doppler examination¹⁵, we measured the peak systolic velocity (PSV) of the venous flow, although it might have been more appropriate to measure instead the mean blood flow velocity (MV) for the IJV. However, as superficial veins flow is not modulated by breathing, the PSV is equivalent to the MV. Using these methods, our study is the first to describe that healthy patients had a similar right and left PSV for all superficial veins studied, with always antegrade flows, whereas patients with previous ligatures had some significant right/left differences.

The investigation of the anatomy and physiology of the cervico-facial venous system is difficult owing to numerous intra- and inter-individual anatomical variations¹⁶, and to multiple venous anastomoses between the superficial and deep facial venous system, and the extracranial and intracranial venous system^{17,18,19,20}. Cerebral venous drainage in the cervico-facial veins also varies depending on body position²¹. Indeed in the supine position, the IJV represents the main route for cerebral venous drainage, whereas in the upright position, owing to the collapse of the IJV, most of the cerebral venous drainage is carried out by extrajugular venous pathways^{21,22}. Venous return is also altered by the pressure gradients of blood flow into the thorax, resulting from respiratory variations and intrathoracic pressures²².

Under physiological conditions, the venous blood flow of neck veins (IJV and subclavian vein) studied by Doppler-ultrasound, has been reported by Pucheu et al. to be symmetrical and biphasic in 57% of cases, continuous in 29% of cases, and monophasic in 13% of cases²³. Flow velocities are reported to be low (< 1 m/s) with large individual variations²³. The diameter of the neck veins (IJV and subclavian vein) also varies according to the patient's position and respiration²³. The global symmetry of the diameter and blood flow described for deep veins of the neck²³ also appears to exist in the superficial venous system of the face in physiological conditions in our serie.

However, the ligation of main venous collector trunks can generate a redistribution of venous blood flow to alternative collateral pathways⁴⁵. The ability of the venous system to compensate for obstruction to its major channels, is well illustrated in case of bilateral radical neck dissection with excision of the jugular veins²⁴. The overall complication rate being lower for staged or delayed second radical neck dissection compared to simultaneous radical neck dissection²⁵. It is supposed that the redistribution of venous blood flow to alternative collateral pathways takes 3 to 4 weeks, and is conditioned by the number and size of existing anastomoses and collaterals²⁴.

In our serie of patients, a redistribution of venous blood flow on the contralateral side of the face and neck seems to occur in case of unilateral ligation of the EJV, as the PSV was significantly increased on the contralateral side of the ligation in group Uext and Uext + Uint. The PSV was also significantly different between the right and left side of the neck for the IJV, in case of bilateral ligation of the EJV. The bilateral ligation of the EJV might consequently disturb the global symmetry of venous blood flow observed in normal neck veins, due to an uneven redistribution of venous blood in the deep venous system of the face and the pterygoid plexuses. Other imaging techniques might be able to explore the deep venous system of the face and confirm that hypothesis²⁶.

The physiological direction of venous blood flow in the cervico-facial venous system still remains hypothetical⁶, and is mostly based on the orientation of the venous valves²⁷. However, it is supposed to have an antegrade direction, and to flow away from the head towards the heart through major venous collector trunk, as observed in our control group. The competency of the head and neck venous valves remains moreover largely unknown, a certain degree incompetency appearing to exist^{28,29,30}. Indeed, IJV valve incompetence is frequently seen in patients with an elevated central venous pressure²². Jugular venous branches reflux is also significantly associated with IJV valve incompetence, and greater IJV blood-flow volume²². In venous segments with existing venous valves, venous reflux requires a reversed pressure gradient and an incompetent venous valve connecting both poles of the pressure gradient²². However, in venous segments without existing venous valves, just a reversed pressure gradient could produce venous reflux²².

Our study is the first to describe the existence of retrograde flows in the superficial veins of the face after venous ligations. The plasticity of the extra-cranial venous system is well-illustrated by numerous descriptions of successful reverse-flow flaps depending on cervico-facial vessels^{31,32,33}. This might explain partially the frequently observed retrograde flows (4 among 24 patients) in the STV, the FV and the IJV in our small series. Further study evaluating the variations of direction and the PSV of venous blood flow in the superficial veins of the face before and months after main collecting trunk ligations, should confirm the existing correlation between venous trunk ligations and retrograde flow in superficial veins of the face.

Finally, there is no way to predict if the flow is going to be retro or antegrade when the patients experienced previous ligations of the main vessels knowing only their surgical history, since patients with the same types of ligation may have either antegrade or retrograde flows in their superficial veins. One should therefore be cautious when planning

microvascular anastomoses on superficial veins of a previously operated neck, and a systematic pre-operative Doppler-ultrasound may be useful to evaluate the hemodynamic parameters of the remaining recipient arteries but also veins. Another solution, when both sides are available for anastomosis, would be to prefer the side where no ligation has been performed when considering anastomosis on a superficial cervico-facial vein.

CONCLUSION :

These results show that a reverse flow is frequently observed in the superficial veins of the face when previous ligations of major cervical veins have been performed. A better understanding of the normal and pathological physiology of the cervico-facial venous system could help the head and neck microsurgeon to reduce the risk of venous insufficiency and thrombosis, in case of free flap surgery of the head and neck.

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FIGURE LEGENDS :

Figure 1: Color-Doppler Ultrasound of the left superficial temporal vein (in blue).

Table 1 : Healthy volunteers and patients characteristics.

Table 1.A: Healthy volunteers

HBP : high blood pressure, BMI : body mass index, DVT : deep venous thrombosis, PAOD : peripheral artery occlusive disease

Table 1.B: Patients characteristics (group Bext, Uext and Uext + Uint).

HBP : high blood pressure, BMI : body mass index, DVT : deep venous thrombosis, PAOD : peripheral artery occlusive disease

Table 2: Hemodynamic parameters of the superficial veins of the face in the healthy volunteers and patients population.

Table 2.A: Hemodynamic parameters of the superficial temporal vein

STV: superficial temporal vein, PSV: peak systolic speed

Table 2.B: Hemodynamic parameters of the facial vein

FV: facial vein, PSV: peak systolic speed

Table 2.C: Hemodynamic parameters of the internal jugular vein

IJV: internal jugular vein, PSV: peak systolic speed, Bilateral: antegrade flow during the systole, and retrograde flow during the diastole

Table 1.A :

	Healthy volunteers group (n = 10)
Mean age (years):	34 (27-40)
Sex :	
Female	5
Male	5
Cardiovascular risk factors:	
Diabetes mellitus	0
HBP	0
Tobacco	3
Impaired renal function	0
Dyslipidemia	0
BMI > 25	1
Cardiovascular history:	
Cardiac disease	0
Cerebrovascular accident	0
DVT	0
PAOD	0

Table 1.B :

	Group Bext (n = 8)	Group Uext (n = 8)	Group Uext + Uint (n = 8)
Mean age (years):	62 (33-74)	58 (28-73)	69 (61-76)
Sex :			
Female	2	3	1
Male	6	5	7
Cardiovascular risk factors :			
Diabetes mellitus	1	1	3
HBP	2	2	3
Tobacco	5	8	4
Impaired renal function	1	1	2
Dyslipidemia	0	1	0
BMI > 25	0	1	3
Cardiovascular history:			
Cardiac disease	0	0	2
Cerebrovascular accident	0	2	0
DVT	0	0	1
PAOD	1	0	1
Tumor site :			
Oral cavity	2	5	3
Oropharynx	3	2	2
Larynx/Hypopharynx	3	0	2
Cervical lymph node without primary	0	1	1
Mean time period between surgery and Doppler-ultrasound (years) :	3 (0,7-6,6)	3,3 (0,7-12,5)	3,3 (0,1-11,5)
Adjuvant treatment:			
Radiation therapy	7	7	6
Chemotherapy	4	3	6

Table 2.A :

	Healthy volunteers group (n = 10)			Group Bext (n = 8)		
	STV (n = 10)		t-Student for paired data	STV (n = 7)		t-Student for paired data
	Right	Left		Right	Left	
Diameter (mm)	1,4 [range : 0,6 – 1,6]	1,2 [range : 0,5 – 1,9]	1	1,5 [range : 0,3 – 2,1]	1,4 [range : 0,5 – 2,2]	0,549
PSV (cm/s)	16,6 [range : 5 – 28]	15,4 [range : 9,6 – 32]	0,499	19,9 [range : 9,2 – 19,9]	9,5 [range : 6,6 – 29,1]	0,385
Flow direction	Antegrade (n=10)	Antegrade (n=10)		Antegrade (n=7)	Antegrade (n=7)	
	Group Uext (n = 8)			Group Uext + Uint (n = 8)		
	STV (n = 8)		t-Student for paired data	STV (n = 8)		t-Student for paired data
	Ipsilateral	Contralateral		Ipsilateral	Contralateral	
Diameter (mm)	1,8 [range : 0,9 – 3,1]	1,5 [range : 0,9 – 2,4]	0,474	1,2 [range : 0,5 – 1,5]	1,3 [range : 0,7 – 2,3]	0,037
PSV (cm/s)	12,4 [range : 5 - 32]	25,4 [range : 5 - 41]	0,014	6,5 [range : 5 – 27,1]	27,3 [range : 5,3 – 33,4]	0,017
Flow direction	Antegrade (n=8)	Antegrade (n=8)		Antegrade (n=8)	Antegrade (n=7)/ Retrograde (n=1)	

Table 2.B :

	Healthy volunteers group (n = 10)			Group Bext (n = 8)		
	FV (n = 10)		t-Student for paired data	FV (n = 4)		t-Student for paired data
	Right	Left		Right	Left	
Diameter (mm)	1,7 [range : 0,5 – 3,3]	1,5 [range : 0,7 – 2,3]	0,424	1,7 [range : 0,9 – 2,9]	1,4 [range : 1,2 – 1,8]	0,346
PSV (cm/s)	30,9 [range : 5 – 59,6]	22 [range : 11,9 – 39,8]	0,205	23,1 [range : 22,3 – 55,2]	25,9 [range : 16,7 – 56,6]	0,994
Flow direction	Antegrade (n=10)	Antegrade (n=10)		Antegrade (n=3) Retrograde (n=1)	Antegrade (n=3) Retrograde (n=1)	
	Group Uext (n = 8)			Group Uext + Uint (n = 8)		
	FV (n = 7)		t-Student for paired data	FV (n = 4)		t-Student for paired data
	Ipsilateral	Contralateral		Ipsilateral	Contralateral	
Diameter (mm)	2,3 [range : 1,4 – 8,3]	3 [range : 1,4 – 5,3]	0,830	2 [range : 0,9 – 2,2]	2 [range : 1,2 – 2,1]	0,711
PSV (cm/s)	20 [range : 8,2 – 29,5]	42,7 [range : 14,4 – 80]	0,143	13,5 [range : 7,5 – 18]	24,9 [range : 9,3 - 54]	0,279
Flow direction	Antegrade (n=4)	Antegrade (n=4)		Antegrade (n=4)	Antegrade (n=3) Retrograde (n=1)	

Table 2.C :

	Healthy volunteers group (n = 10)			Group Bext (n = 8)		
	IJV (n = 10)		t-Student for paired data	IJV (n = 8)		t-Student for paired data
	Right	Left		Right	Left	
Diameter (mm)	13,5 [range : 7,2 – 17,1]	11,1 [range : 4,5 – 17,3]	0,287	10 [range : 7,7 – 15,5]	9 [range : 8,6 – 10,8]	0,018
PSV (cm/s)	35,7 [range : 31 – 103]	49 [range : 19,9 – 113]	0,499	50 [range : 32 – 96,2]	25 [range : 10,8 – 61,3]	0,047
Flow direction	Antegrade (n=10)	Antegrade (n=10)		Antegrade (n=8)	Antegrade (n=7) Bilateral (n=1)	
	Group Uext (n = 8)			Group Uext + Uint (n = 8)		
	IJV (n = 8)		t-Student for paired data	IJV (n = 8)		
	Ipsilateral	Contralateral		Ipsilateral	Contralateral	
Diameter (mm)	8,6 [range : 3 – 11,7]	10 [range : 4,3 – 17,3]	0,243	-	11,6 [range : 6 – 18,1]	-
PSV (cm/s)	31 [range : 13,2 – 72]	50,7 [range : 10 – 74,5]	0,031	-	33 [range : 13,2 – 70]	-
Flow direction	Antegrade (n=8)	Antegrade (n=8)		-	Antegrade (n=8)	