Le reazioni vasovagali: strategie per la prevenzione e compliance del donatore

Vasovagal reactions: strategies for prevention and blood donor compliance

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Definition

Vasovagal syncope (VVS) is transient loss of consciousness due to a sudden drop of blood pressure (BP) caused by reflex: peripheral vasodilatation combined with bradycardia.

→ Vasovagal syncope is a common condition in the general population

Definition

Syncope, Vasovagal **Mesh term:**

"Loss of consciousness due to a reduction in blood pressure that is associated with an increase in vagal tone and peripheral vasodilation".

Year introduced: **1997**

VVRS

- **Isolated vasovagal syncope** (VVS) is not a disease, but rather, the clinical manifestation of an autonomic reflex predisposed in all (or almost all) individuals

- **VVRs** range from mild pre-syncopal symptoms (e.g. nausea and light-headedness) to severe reactions involving syncope.

The term **‘pre-syncope’or ‘near-syncope**’ is used to describe a state that resembles the prodrome of syncope but which is **not followed by loss of consciousness (LOC)**

The pathophysiology of VVS

Reflex activation  rapid decrease

- heartbeat
- vascular tone

Classification

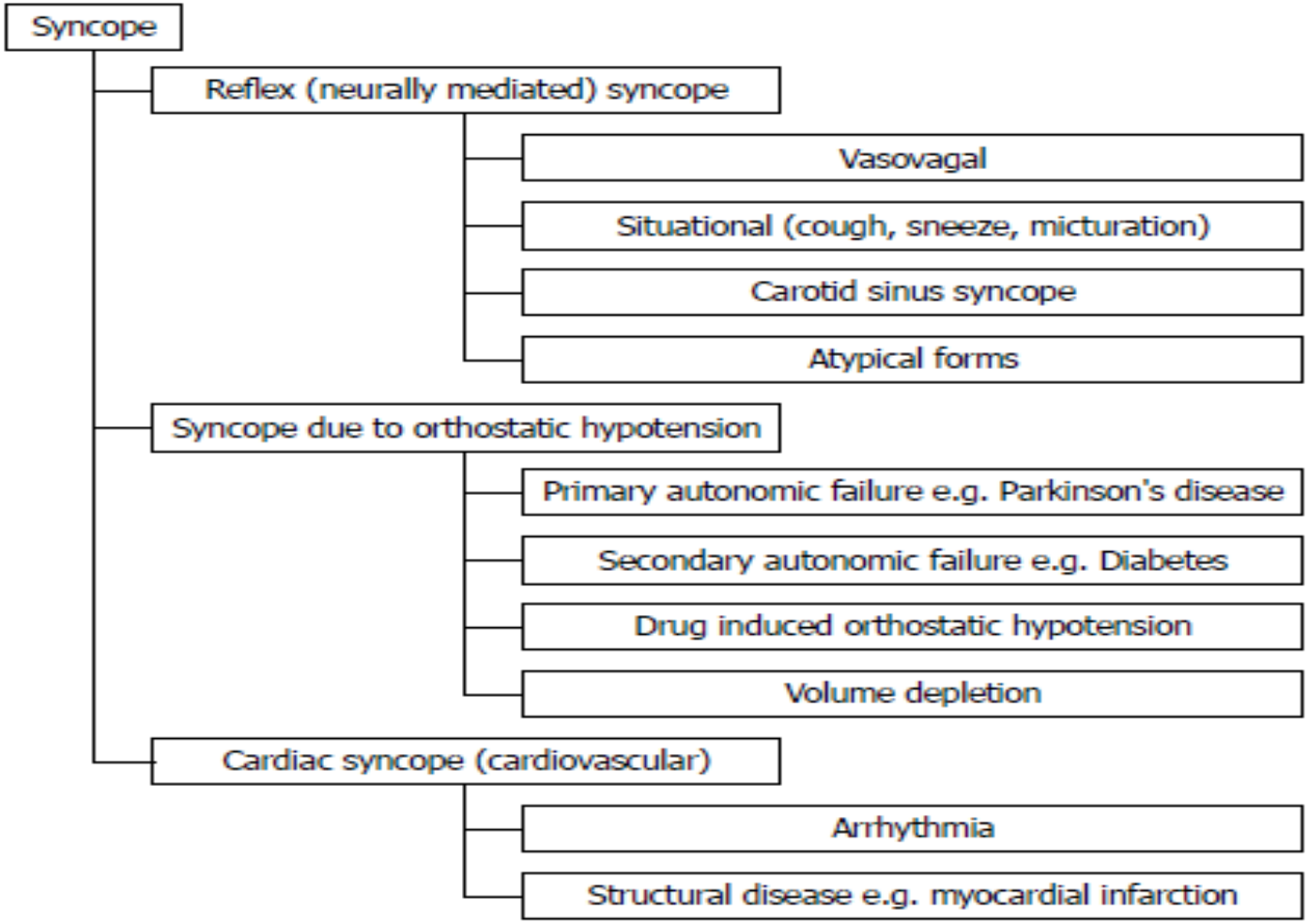

Figure 1 Classification of syncope.

Italian Blood System 2016: activity data, haemovigilance and epidemiological surveillance. Volume 1. Liviana Catalano et al.

Italian National Blood Centre

Table 26. Adverse reactions to donations classified per severity level (2016)

Adverse reaction	Mild	%	Moderate	%	Severe	%
Immediate vasovagal reaction	5,248	79.4	1,126	17.0	239	3.6
Delayed vasovagal reaction	789	70.8	252	22.6	73	6.6
Haematoma		0.0		0.0	684	100.0
Citrate paraesthesia/tingling	184	74.2		0.0	64	25.8
Tightness in the chest	1	100.0		0.0		0.0
Arterial puncture		0.0	23	88.5	3	11.5
Arteriovenous fistula		0.0		0.0	2	100.0
Incidents tied to vasovagal syndrome		0.0		0.0	19	100.0
Nerve injury due to a haematoma		0.0	2	100.0		0.0
Nerve injury	8	88.9	1	11.1		0.0
Systemic allergic reaction		0.0		0.0	5	100.0
Local allergic reaction		0.0		0.0	5	100.0
Cold/shivers	14	63.6		0.0	8	36.4
Citrate tetany		0.0		0.0	7	100.0
Thrombophlebitis		0.0		0.0	8	100.0
Other incidents	27	87.1	4	12.9		0.0
Other	143	84.6	21	12.4	6	3.0
Total	**6,414**	**71.5**	**1,429**	**15.9**	**1,123**	**12.5**

VVRs

TABLE 1. Signs and Symptoms of Vasovagal Reactions

Signs	*Symptoms*
Pallor (79%)	Faintness and dizziness (85%)
Sweating (57%)	Nausea (50%)
Shivering	Heat intolerance (31%)
Vomiting	Cold intolerance (21%)
Loss of consciousness	

VVRs Reaction codes

TABLE 1. Phlebotomist-rated donor reaction codes

None	Mild	Moderate	Severe
	• Pallor (skin color change) • Feeling faint, lightheaded, dizzy, sweating • Hyperventilating (rapid breathing), may complain of fingers tingling • Pale, nauseated, stomach cramping	In addition to all or some of the mild signs and symptoms: • Momentary loss of consciousness ≤ 45 sec • Vomiting and/or incontinence	In addition to all or some of the signs and symptoms for mild/moderate reaction: • Tetany spasms • Convulsions • Confusion • Loss of consciousness >45 sec • Recovery from mild or moderate symptoms lasting >30 min

VVRs

Table 1. Vasovagal symptoms by reaction severity

Reaction category	Symptoms
Pre-syncopal (mild)	Light-headedness, pallor, dizziness, sweating, fatigue, blurred and fading vision, difficulty hearing, palpitations, nausea and/or vomiting
Syncope (severe)	Loss of consciousness

Genetic architecture of syncope

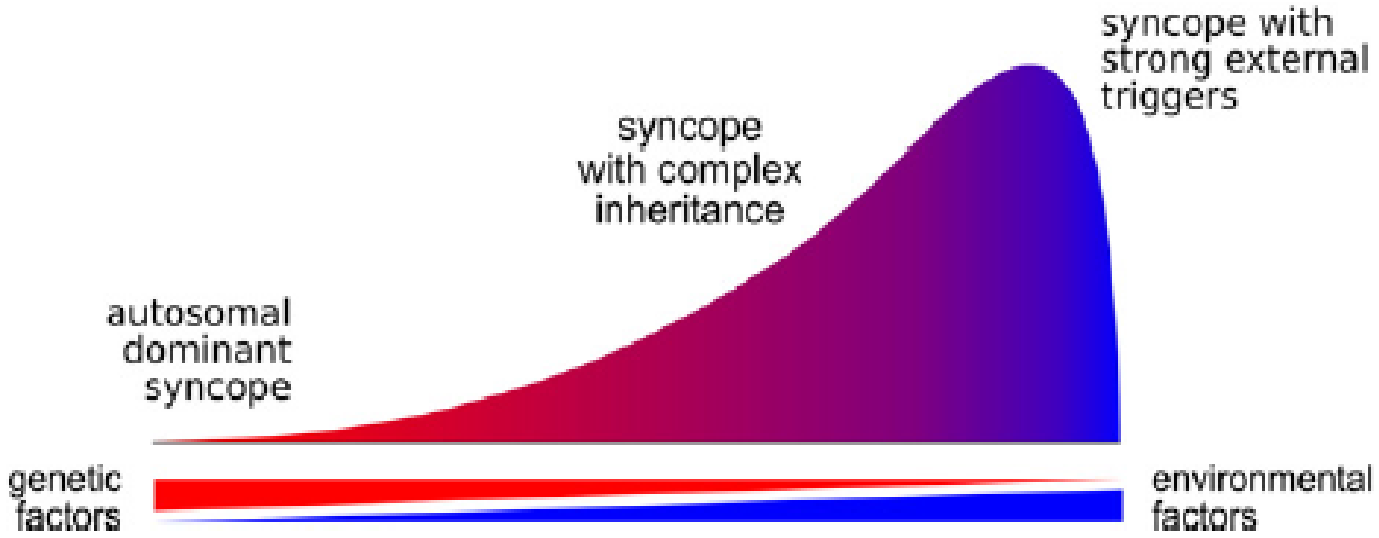

Fig. 2. Conceptualization of the genetic architecture of syncope. The x axis shows the spectrum of syncope with predominant genetic factors on the left and predominant external factors on the right. The y axis shows the assumed frequency of the different forms. Syncope due to strong environmental triggers where genetic factors are less relevant is assumed to be most frequent. Autosomal dominant vasovagal syncope is least common.

(Klein KM, Autonomic Neuroscience: Basic and Clinical, 2014)

Possible genetic association

Examined genes and result of association (+/—)

— *ACE*
+ *ADRB1* tilt test result
+ *GNB3* "typical vasovagal history"
+ *GNAS1* tilt test result
— *GNB3*
+ *ADRB1* tilt test result
— *GNAS1*
+ *GNB3* tilt test result
— *RGS2*
+ *EDN1* tilt test result
— *EDNRA*
— *GNAS1*
— *GNB3*
— *RGS2*
+ *ADORA2A* tilt test result, number of syncopal episoc
— *ACE*
— *AGT*
— *ATR1*
— *SERT*
+ *RGS2* number of syncopal episodes
— *ADRA1A*
— *ADRB1*
— *ADRB2*
— *DBH*
— *GNB3*
— *SERT*
— *CHRM2*
— *GNB1*
— *GNG2*
— *KCNJ3*
+ *KCNJ5* VVS with positive tilt test result
+ *ADRA1A* tilt test result

VVRs

1) VVRs **more frequently whole blood (WB)** donation than for other forms of blood product donation at needle removal/leaving chair (Crocco *et al.,* 2009; Tomasulo *et al*. 2010).
   Incidence of **pre-syncopal** reactions for WB donations: **1·4–7%, vasovagal syncope**: **0·1–0·5%** (Amrein *et al,* 2012)

2) Apheresis-type donations more common in platelet donations **(0·68–0·81%)** compared to plasma donations **(0·16%)** (Despotis *et al,* 1999; Crocco *et al.* 2009*)*

3) **9/12%** of VVRs occur after the donor have left the Centre (Kamel *et al*. 2010)

VVRs

VVRs have significant implications for

- the welfare of donors
- staff time and training
- the management of donor sessions

most crucially on the retention of donors and security of the blood supply

(France *et al.*, 2004; France *et al.*, 2005; Newman *et al.*, 2006a; van Dongen *et al.*, 2013)

VVRs

Non-return rate for subsequent donation **of 45%** in first-time donors who experience VVRs compared with **18%** in donors who did not experience such reactions, with similar differences in repeat donors

(Wiersum-Osselton *et al.*, 2014)

VVRs trigger

VVRs triggered by various

physical (e.g. standing up after losing 500mL of blood)

psychological stimuli (e.g. pain, stress, fear)

(Gilchrist *et al.,* 2015)

Risk factors for VVRs

Factors linked to a VVR **during** or **after** blood donation

three categories

- donor characteristics that are **generally observable** (e.g. gender, ethnicity)
- donor characteristics that may **not be immediately observable** without additional questioning or assessment (e.g. prior night sleep duration, fear of needles)
- **contextual features** of the donation experience (e.g. wait time, phlebotomist experience

Table 2. Summary of findings of risk factors for VVRs in blood donation

Phlebotomy type	Observable donor characteristics	Unobservable donor characteristics	Contextual factors
Whole blood	Young age	Low blood pressure	Spring season
	First-time donors	Elevated pulse	Less experienced phlebotomist
	Female	Less sleep duration	Lower phlebotomist social skills
	White donors	Greater time after eating	Longer wait time
	Low BMI/weight	Less caffeine intake	Longer bleed time
	Low estimated blood volume	History of VVR	Witnessing a VVR
		Greater anxiety	
		Greater anticipated anxiety	
		Greater fear of blood and injury	
		Greater fear of blood draw	
		Pain	
		Anticipated pain	
		Anticipated disgust	
		Perceived blood loss	
Apheresis	Young age	Elevated pulse	
	First-time donors	Less sleep duration	
	Female	Greater time after eating	
	Low BMI		
	Low estimated blood volume		

Contextual features

- Importance of the phlebotomist in the experience of VVRs (Stewart *et al.* 2006)

- VVRs were more frequent in the spring and least common in the summer. 10 547 Japanese donors (Ogata *et al.* 1980)

- Donors waiting more than **60min** from registration to the beginning of phlebotomy **four times** more reactions who waited **19 min or less.** (France, 2016)

Fear and time

TABLE 2. Percentage of vasovagal reactions observed as a function of donor fear and blood draw time*

Draw time (min)	No Fear	Fear	All donors
<6	5.0 (30/605)	15.7 (33/210)	7.7 (63/815)
≥6 to <8	6.4 (34/529)	16.1 (39/242)	9.5 (73/771)
≥8 to <10	8.5 (19/224)	23.1 (31/134)	14.0 (50/358)
≥10	10.0 (52/522)	31.2 (79/253)	16.9 (131/775)
All donors	7.2 (135/1880)	21.7 (182/839)	11.7 (317/2719)

* Data are reported as percent (number).

France *et al.* Transfusion 2016

Preventing VVRs

Physiological strategies

- Primary objective is to prevent sudden drop in blood pressure

1) Pre-donation water loading

2) AMT (applied muscle tension)

3) Caffeine consumption

Physiological strategies

Pre-donation water loading

5 RCT

500 ml water within 30 min *(Fisher et al. 2016)*

- **No significant** relative risk inVVRs.
- **Reduced** the severity of VVRs

500 ml water 9 min. before

- Significant lower odds of VVR *(Morand et al. 2016)*

Beneficial effects of dietary sodium on increasing plasma volume and orthostatic tolerance *(Weiling et al. 2011)*

The impact of consuming 500 mL **isotonic drink** before phlebotomy. **No differences** *(Morand et al.2016)*

Physiological strategies

AMT (applied muscle tension to increase blood pressure)
Donors engaging in repeated contractions of muscles (legs and abdomen); 8 trials
(Fisher et al. 2016)
No difference in relative VVRs risk
Impact on severity

2 trials combining AMT e water loading *(France et al. 2010)*
significant lower risk phlebotomist-registered VVRs and lower donor self-reported symptom severity *(Morand et al. 2016)*

Pysiological strategies

Consumption of caffeine increases donor blood pressure

1 randomised trial with high-risk donors (62 young females with a sensitivity to blood or injury stimuli)

125 or 250mg of caffeine administered prior to blood donation vs placebo resulted in a significantly lower number of chair reclines, *(Sauer & France, 1999)*

no difference in pre-donation anxiety or increased heart rate

Psychological strategies

Emotion regulation to reduce stress or anxiety
(distraction or social support during the procedure)

Efficacy of audio-visual distraction for first-time donors *(Bonk et al.2001)*

- **Monitoring coping style**
- **Blunting coping style (**significant lower self-reported VVs)

Psychological strategies

- **In situ social support** (self-reported lower levels of VVRs and strong intentions to donate again *(Hanson & France 2009)*

- **Pairing donors** with a **research assistant** trained to be supportive (Stewart *et al.,* 2006) small randomised controlled trial with novice donors (*n*=65)

Phisyological and psycological strategies

large number of intervention studies

- Proposed methods of prevention have **not been standardised** in evaluations (e.g. AMT), and outcomes have been **inconsistently assessed**.
- Impact of VVRs prevention techniques on reducing VVRs in plasmapheresis and plateletpheresis donors **not yet clear**
- Rates of VVRs are **lower** in apheresis donors *(Crocco et al., 2009)*
- All published intervention trials have **focused solely** on WB donors.

Managing the impact of VVRs

Little research has been conducted on how to best manage the physiological and psychological impact of experiencing a VVRs

1) Trendelenburg position to increase central blood volume and cardiac output, minimal increase *(Weiling et al 2011)*

2) Physical stimulation

3) Saline solution (to expand circulation)

4) Corticosterod is not useful

5) Supplement physical manoeuvres providing cold water, something to eat or by placing a cool cloth on the donor's forehead *(Wieling et al, 2011b;Thijsen et al, 2016).*

These techniques are not documented to have a physiological impact but the perception that **something is being done may be beneficial.**

Managing the impact of VVRs

Pharmacological therapy

A number of drugs have been tested in the treatment of vasovagal syncope

- β-blockers,
- disopyramide,
- scopolamine,
- theophylline,
- ephedrine,
- etilefrine,
- midodrine,
- clonidine
- serotonin reuptake inhibitors

no convincing data

Impact of VVRs on donor return

- Immediate negative impact
- Longer-term negative impact for BCAs as they reduce donor return rates
- **VVRs have the strongest deterrent effect of all forms of phlebotomy trauma** *(Veldhuizen et al., 2012)*
- Reducing return rates by **20%** for first-time donors and by **33%** for repeat donors *(France et al. 2014)*

Impact of VVRs on donor return

Rates of donor return after the experience of a VVR are not constant across demographic categories.

Male donors experience **fewer VVRs**, they are **less likely to return** following a reaction compared to female donors (van

(Dongen et al., 2013)

Impact of VVRs on donor return

Contrary to donor beliefs

The risk of **a recurrent event** in WB donation is only **2%** of all VVRs observed on return donation occurring in donors with a prior reaction (Eder *et al.,* 2012)

Important to communicate this low risk of VVRs to donors and provide education

Take home message

- Identification of most vulnerable donors (great attention of the physician)
- Modification of environmental risk factors (clear and calm rooms etc.)
- Removal of human risk factors (expert and compliant personnel)

Prevention
Information