

Postpartum Hemorrhage: Are There Physiological Mechanisms of Prevention?

Antonio Belpiede^{1,2}, Antonio Malvasi^{3,4}, Michael Stark⁵, Andrea Tinelli^{4,6,7,8}

¹ Coordinator of the Apulia Region Birth Points Committee, former Head of the Mother and Child, Italy

² Department ASL BT and Director of Department of Obstetrics and Gynecology of Barletta Hospital, Italy

³ Department of Obstetrics and Gynecology, GVM Care & Research Santa Maria Hospital, Bari, Italy

⁴ Laboratory of Human Physiology, Phystech BioMed School, Faculty of Biological & Medical Physics, Moscow Institute of Physics and Technology (State University), Dolgoprudny, Moscow Region, Russia

⁵ President of the New European Surgical Academy (NESA), Berlin, Germany

⁶ Division of Experimental Endoscopic Surgery, Imaging, Technology and Minimally Invasive Therapy, Vito Fazzi Hospital, Lecce, Italy

⁷ Department of Obstetrics and Gynecology, "Veris delli Ponti" Hospital, Scorrano (Le), Italy

⁸ The Second Affiliated Hospital of Medical College, Xi'an, Jiao Tong University, China

Corresponding author: Andrea Tinelli
andreatinelli@gmail.com

Abstract

The postpartum hemorrhage (PPH) it is one of the worst complications of the pregnant woman and the leading cause of maternal mortality in the world, as it produces potentially catastrophic effects on patients, with high morbidity and mortality. Likewise, the reduction in maternal mortality, which is particularly high in low income countries, but rising even in developed countries (as in USA), is one of the eight primary global health current goals of the WHO. In the complex pathophysiological phenomenon of PPH, the uterine contractility and connective tissue arrangement are poorly investigated. Both topics are scantily little understood and investigated, in terms of pelvic functional anatomy and pathophysiology. The anti-version uterine posture is essential for the optimal and necessary muscle contraction in the immediate postpartum stage, to avoid PPH onset. In this review, authors analyzed the physiology of uterine contraction related to the childbirth and the PPH, identifying an anatomical system involved in the physiological post-partum uterine contraction. This biological system is the integrated pelvic myofascial system and it has a prime importance in the physiological reduction of the PPH risk and to maintain uterine contractility during and after childbirth.

Keywords: Postpartum hemorrhage, uterine contraction, round ligaments, myofascial system, uterine posture.

1. Introduction

The postpartum hemorrhage (PPH) it is unfortunately a relatively widespread and common clinical condition; it is one of the main causes of severe maternal morbidity, causing 150,000 dead patients for year, that is, 25% of the 600,000 annual maternal deaths worldwide (Khan et al. 2006).

Unfortunately, basing on a study, approximately 3% to 5% of pregnant will experience PPH (Knight et al. 2009) and it causes, annually, one-fourth of maternal deaths worldwide (Say et al. 2014).

In developed nations, PPH has fallen to second or third place for direct maternal deaths behind hypertensive and thromboembolic complica-

tions (Khan et al. 2006; Knight et al. 2009; Say et al. 2014), while in high-income countries, 80 to 90% of maternal deaths from PPH may be avoidable for the delayed diagnosis and inadequate treatment (Fawcus 2019).

Beyond the direct consequences of acute hypovolemia, PPH exposes women to the complications of transfusion, resuscitation, infertility when treated by hysterectomy (1 case for 2000-3500 deliveries in developed countries), increased risks of thromboembolic complications, and greater psychological fragility (McNamara and Mallaiah 2019).

From the clinical point of view, the ACOG (American College of Obstetricians and Gynecologists) defines early PPH as at least 1,000 mL total blood loss, or loss of blood coinciding

with signs and symptoms of hypovolemia within 24 hours after delivery of the fetus or intrapartum loss ("ReVITALize Obstetric Data Definitions - ACOG" n.d.). Moreover, primary PPH may occur before delivery of the placenta and up to 24 hours after delivery of the fetus ("ReVITALize Obstetric Data Definitions - ACOG" n.d.).

PPH involves many hospital and university experts and specialists, is the subject of physiology and pathophysiology studies, stimulates pharmaceutical companies to seek new therapies and surgical instrumentation industries to produce devices to solve PPH.

In this review we will analyze the uterine physiology and the pathophysiology involving PPH, trying to evaluate the possibilities of physiological treatment in the resolution of the pathology.

2.1 Physiology of uterine contraction after delivery

Human anatomy is an extremely complex system tending towards semi-perfection, such as the intrinsic characteristics of the uterine muscle, on those of uterine contraction and on the unknown role that it carries out the whole myofascial system and the round ligaments.

The uterine muscle is a unitary smooth muscle differing from the multi-unit smooth muscle, because the contraction is synchronized by communicating junctions, that allow to coordinate the cells contraction (Egarter and Husslein 1992). The smooth muscle, despite having a myosin content of about 20% and a consumption of ATP 100 times lower than the skeletal muscle, can develop the same strength for transverse section area. It happens either for much slower rhythmical contractions, or for an architecture of the smooth muscle cell and the unitary organization of smooth muscle, structured in a syncytium (Egarter and Husslein 1992).

The uterine muscle behaves like a viscous mass and it is also characterized by a tension variability exerted at any given extent, and there is either no relationship between extent and tension, nor between extent and a length of rest (Sosa-Stanley and Peterson 2018).

Thanks to this plasticity, a strip of visceral smooth muscle, when stretched, first exerts a certain tension, but if the stretch is maintained, the tension gradually decreases and can go

down to the initial or even lower level of tension (Sammali et al. 2018).

The uterine tone is a persistent state of partial contraction, showing continuous irregular contractions independent from the innervation and the membrane potential is unstable, with no real resting value (Roger Charles Young 2018)

The viscoelasticity of the uterine muscle is linked to the characteristics of the muscle fibers in the viscous component and to the collagen and elastin for the elastic component (Sammali et al. 2018).

The uterine muscle can, therefore, be considered as a "viscous mass" that needs to be oriented in extension and during contraction, with the lasting crucial role of the round ligaments (Sammali et al. 2018).

2.2 The anatomical role of round ligaments in uterine contractions

The round ligaments are formed by fibers and smooth muscles and, after the passage in the inguinal canals, by striated musculature (from the transversus and oblique abdominal muscles) (Chaudhry and Chaudhry 2019).

The round ligaments in the woman flap off in the labia majora and in the mountain of Venus (even in sexual activity the stimulation of these areas leads to uterine contractions of the orgasm) (Bellier et al. 2018).

The existence of the round ligaments, even if poorly represented, in quadrupeds, that obviously have the belly down and in which gravity favors the anterior position of the uterus, shows that they have more of a role of muscle-nerve terminal than of support (Iwanaga et al. 2016).

From a phylogenetic point of view, it is in women that the round ligament reaches its greatest development and it is not a vestige of the past (Iwanaga et al. 2016)

The round ligament is associated with the standing station and the new reproductive needs linked to this (Bulletti and De Ziegler 2006).

The need arises to anteriorize the uterus for abdominal development during pregnancy that would otherwise be suffocated in the pelvis or crush the large vessels, to make the cervix in the posterior fornix during coitus, but also because a uterus lying backwards in the postpar-

tum does not contract well (Sosa-Stanley and Peterson 2018; Sammali et al. 2018; Roger Charles Young 2018).

The round ligaments are improperly anatomically linked to the pelvic suspension system, because they are real muscles, as they can bear a load of 600 to 900 grams (Chaudhry and Chaudhry 2019).

Moreover, the round ligament is the essential element that determines the orientation of the body of the uterus "like a horse held by the reins" (Chaudhry and Chaudhry 2019).

During pregnancy, the round ligaments become 3 to 4 times thicker and the resistance they offer to traction increases up to 40 kg (Chaudhry and Chaudhry 2019) and, during pregnancy, they move away from the uterine fundus and the "Calza's Bundle" (central longitudinal band that in primates constitutes the neo-myometrium of the uterus, not more bicornate as in the quadrupeds), from which they depart, is more anatomically evident (Kamina, P. Lorenzini 1975).

They orient uterine contraction surely also in labor and there are certainly different types of uterine contraction (Devedeux et al. 1993) with different receptors (or different sensitivity) for each muscular layer (neomyometrium, paleomyometrium and archimiometry) (Sosa-Stanley and Peterson 2018; Sammali et al. 2018; Roger Charles Young 2018).

Nevertheless, during Braxton Hicks contractions or in those in the latent phase of labor, in which the fetal head adapts to birth canal, they are probably not the same muscle fibers that contract in the active phase of labor (Maul et al. 2003) The round ligaments contractions could orient the uterus, adapting to its content and playing an important role during pregnancy and labor (Roger C. Young 2007).

The so called "ligament round pain", poorly diagnosed in Italy, is better known and investigated by Osteopaths than by the Obstetrician.

2.3 *The hypothesis of integrated pelvic myofascial system*

The uterine contraction in the expulsive stage of labor is "detrusor type" and leads to the fetal delivery. The uterine musculature, being in

three layers, has the neo-myometrium (on the fund) that continues with the fibers of the round ligaments (like a Bolivian wool cap) (Escalante, NMM 2017).

In the postpartum uterine contraction, the uterine body is "guided" by the round ligaments, which contracts down and forward, and the lower uterine segment (LUS) contracts towards the pubic symphysis (Chaudhry and Chaudhry 2019).

All the studies on uterine contraction focused on the characteristics of the muscle fiber and on the electric potential of the membrane, rather than on the uterine muscle, structured in a syncytium (Devedeux et al. 1993).

Synthetic oxytocin stimulates the uterine fundal contraction, but not always the round ligaments or, at least, not at the same time and, hence, synthetic oxytocin cannot help the uterine posture (Maul et al. 2003; Roger C. Young 2007).

The first and second line standard pharmacological therapies for PPH, provided for by the national and international guidelines (Evensen, Anderson, and Fontaine 2017; Sentilhes et al. 2016) are less effective in all those situations in which there is an alteration of the myofascial system (obesity, supine position, cesarean section) that does not favor correct posture uterine during contraction (Vallera et al. 2017; Sentilhes et al. 2016).

Currently, in a mechanical-biological vision and with a more organicist anatomic-biological approach, mechanical forces must be considered together, and not only just into the uterine fibromuscular cell, typical of molecular biology.

Hence the hypothesis that the uterine contraction could depend not only by uterine muscle fibers, but by a complex integrated pelvic myofascial system, connecting the uterine muscle to the round ligaments, to the ileo-psoas muscles (via the genital femoral nerve) and to the muscles of the abdominal wall. The "axial fascia" or "deep fascia" (Bordoni and Simonelli 2018) wraps and connects the uterine muscle, its ligaments, the postural muscles in a single interconnected system, that, after delivery, progressively returns to the "status quo ante".

Currently, rethinking to obstetric daily experience in delivery room, it must therefore think to a rearrangement of the whole myofascial sys-

tem, favoring directly the abdominal viscera descent behind the uterus during labor and indirectly the intra-abdominal pressure increase. In the human body architecture, the myofascial system is the anatomical structure that connects the anatomical districts and the human organs in the body (Bordoni and Simonelli 2018). The term "fascia" refers to the collagen-fibrous tissues that are part of a broad system of transmission of tension forces in the human body (Bordoni 2019; Bordoni et al. 2018). The "fascia" appears as an interconnected tension network consisting of the dense and loose connective tissue, from the surface to the depth. The ligaments are local densifications of this network. There is an extended continuity of the fibrous tissue, and the collagen tissue expresses a gradual transition. So, it is impossible to make a clear distinction between the ligament and the loose part of the intra-abdominal and pelvic fascia (Bordoni and Simonelli 2018; Bordoni 2019; Bordoni et al. 2018). The fascial body therefore represents, within the human body, a wide anatomical structure with structural and functional network functions, consisting of bags, ropes (local densifications), thousands of cavities inside other cavities, all connected by robust or soft septa (Bordoni et al. 2019; Bordoni and Zanier 2014; Bordoni and Lagana 2019). The "visceral fascia" consists of collagen and elastic fibers and covers the body cavities (Bordoni et al. 2019). The bands wrapping the organs are called pleura, peritoneum, sheath, but they remain visceral bands (Bordoni and Simonelli 2018; Bordoni 2019; Bordoni et al. 2018, 2019). Very interesting is the significant increase in the risk of postpartum hemorrhage in Ehlers Danlos syndrome, characterized by severe connective tissue disorders. In fact, pregnant women with Ehlers Danlos syndrome experienced postpartum hemorrhage (19% vs. 7%) more often than the unaffected women (Lind and Wallenburg 2002).

3. Conclusions

There is a "global range" that, during pregnancy, is subject to mechanical tensions gradually increasing both from the growing fetus and from the pressures of the maternal uterus. The

abdominal diaphragm has a sort of dome turned upside down. The pelvic diaphragm upwards and these two muscle groups are located at the upper and lower extremities of the peritoneal cavity which, like a balloon, encloses the abdominal organs. The transmission of pressure takes place inside (intra-abdominal) and outside (abdominal and trunk muscles) of this balloon and it is transmitted to all the abdominal organs, by an integrated pelvic myofascial system. This biological system should be adequately investigated for its fundamental importance in its ability to physiologically reduce the risk of PPH and to maintain uterine contractility during and after childbirth.

References

- Bellier, A, G Cavalié, G Marnas, and P Chaffanjon. 2018. "The Round Ligament of the Uterus: Questioning Its Distal Insertion." *Morphologie : Bulletin de l'Association Des Anatomistes* 102 (337): 55–60. <https://doi.org/10.1016/j.morpho.2018.04.001>.
- Bordoni, Bruno. 2019. "Improving the New Definition of Fascial System." *Complementary Medicine Research*, December. <https://doi.org/10.1159/000500852>.
- Bordoni, Bruno, and Maria Marcella Lagana. 2019. "Bone Tissue Is an Integral Part of the Fascial System." *Cureus*, January. <https://doi.org/10.7759/cureus.3824>.
- Bordoni, Bruno, Fabiola Marelli, Bruno Morabito, Roberto Castagna, Beatrice Sacconi, and Paul Mazzucco. 2018. "New Proposal to Define the Fascial System." *Complementary Medicine Research* 25 (4): 257–62. <https://doi.org/10.1159/000486238>.
- Bordoni, Bruno, and Marta Simonelli. 2018. "The Awareness of the Fascial System." *Cureus*, October. <https://doi.org/10.7759/cureus.3397>.
- Bordoni, Bruno, Stevan Walkowski, Bruno Morabito, and Matthew A Varacallo. 2019. "Fascial Nomenclature: An Update." *Cureus* 11 (9): e5718. <https://doi.org/10.7759/cureus.5718>.
- Bordoni, Bruno, and Emiliano Zanier. 2014. "Clinical and Symptomatological Reflections: The Fascial System." *Journal of Multidisciplinary Healthcare* 7: 401–11. <https://doi.org/10.2147/JMDH.S68308>.
- Bulletti, Carlo, and Dominique De Ziegler. 2006. "Uterine Contractility and Embryo Implantation." *Current Opinion in Obstetrics and*

- Gynecology*.
<https://doi.org/10.1097/01.gco.0000233947.97543.c4>.
- Chaudhry, Shazia R., and Khalid Chaudhry. 2019. *Anatomy, Abdomen and Pelvis, Uterus Round Ligament*. StatPearls.
 - Devedeux, Dominique, Catherine Marque, Souheil Mansour, Guy Germain, and Jacques Duchêne. 1993. "Uterine Electromyography: A Critical Review." *American Journal of Obstetrics and Gynecology* 169 (6): 1636–53. [https://doi.org/10.1016/0002-9378\(93\)90456-S](https://doi.org/10.1016/0002-9378(93)90456-S).
 - Egarter, C. H., and P. Husslein. 1992. "4 Biochemistry of Myometrial Contractility." *Bailliere's Clinical Obstetrics and Gynaecology* 6 (4): 755–69. [https://doi.org/10.1016/S0950-3552\(05\)80187-7](https://doi.org/10.1016/S0950-3552(05)80187-7).
 - Escalante, NMM, Pino JH. 2017. "Arrangement of Muscle Fibres in the Myometrium of the Human Uters: A Mesoscopic Study." *MOJ Anat. Physiol* 4 (2): 280–83.
 - Evensen, Ann, Janice M. Anderson, and Patricia Fontaine. 2017. "Postpartum Hemorrhage: Prevention and Treatment." *American Family Physician* 95 (7): 442–49.
 - Fawcus, Susan. 2019. "Practical Approaches to Managing Postpartum Haemorrhage with Limited Resources." *Best Practice & Research. Clinical Obstetrics & Gynaecology* 61 (November): 143–55. <https://doi.org/10.1016/j.bpobgyn.2019.03.009>.
 - Iwanaga, Ritsuko, David J Orlicky, Jameson Arnett, Marsha K Guess, K Joseph Hurt, and Kathleen A Connell. 2016. "Comparative Histology of Mouse, Rat, and Human Pelvic Ligaments." *International Urogynecology Journal* 27 (11): 1697–1704. <https://doi.org/10.1007/s00192-016-3008-6>.
 - Kamina, P. Lorenzini, D. 1975. "Anatomia Ginecologia e Ostetrica: Organogenesi, Descrizione, Elaborazione." *Mapparese- DEMI*.
 - Khan, Khalid S., Daniel Wojdyla, Lale Say, A. Metin Gülmezoglu, and Paul FA Van Look. 2006. "WHO Analysis of Causes of Maternal Death: A Systematic Review." *Lancet* 367 (9516): 1066–74. [https://doi.org/10.1016/S0140-6736\(06\)68397-9](https://doi.org/10.1016/S0140-6736(06)68397-9).
 - Knight, Marian, William M. Callaghan, Cynthia Berg, Sophie Alexander, Marie Helene Bouvier-Colle, Jane B. Ford, KS S. Joseph, et al. 2009. "Trends in Postpartum Hemorrhage in High Resource Countries: A Review and Recommendations from the International Postpartum Hemorrhage Collaborative Group." *BMC Pregnancy and Childbirth* 9 (November). <https://doi.org/10.1186/1471-2393-9-55>.
 - Lind, J., and H. C.S. Wallenburg. 2002. "Pregnancy and the Ehlers-Danlos Syndrome: A Retrospective Study in a Dutch Population." *Acta Obstetrica et Gynecologica Scandinavica* 81 (4): 293–300. <https://doi.org/10.1034/j.1600-0412.2002.810403.x>.
 - Maul, Holger, William L. Maner, George R. Saade, and Robert E. Garfield. 2003. "The Physiology of Uterine Contractions." *Clinics in Perinatology*. W.B. Saunders. [https://doi.org/10.1016/S0095-5108\(03\)00105-2](https://doi.org/10.1016/S0095-5108(03)00105-2).
 - McNamara, Helen, and Shuba Mallaiah. 2019. "Managing Coagulopathy Following PPH." *Best Practice & Research. Clinical Obstetrics & Gynaecology* 61 (November): 106–20. <https://doi.org/10.1016/j.bpobgyn.2019.04.002>.
 - "ReVITALize Obstetric Data Definitions - ACOG." n.d. Accessed January 28, 2020. <https://www.acog.org/About-ACOG/ACOG-Departments/Patient-Safety-and-Quality-Improvement/reVITALize-Obstetric-Data-Definitions?IsMobileSet=false>.
 - Sammali, Federica, Nienke Pertronella Maria Kujsters, Benedictus Christiaan Schoot, Massimo Mischi, and Chiara Rabotti. 2018. "Feasibility of Transabdominal Electrohysterography for Analysis of Uterine Activity in Nonpregnant Women." *Reproductive Sciences (Thousand Oaks, Calif.)* 25 (7): 1124–33. <https://doi.org/10.1177/1933719118768700>.
 - Say, Lale, Doris Chou, Alison Gemmill, Özge Tunçalp, Ann Beth Moller, Jane Daniels, A. Metin Gülmezoglu, Marleen Temmerman, and Leontine Alkema. 2014. "Global Causes of Maternal Death: A WHO Systematic Analysis." *The Lancet Global Health* 2 (6). [https://doi.org/10.1016/S2214-109X\(14\)70227-X](https://doi.org/10.1016/S2214-109X(14)70227-X).
 - Sentilhes, Loïc, Benjamin Merlot, Hugo Madar, François Sztark, Stéphanie Brun, and Catherine Deneux-Tharaux. 2016. "Postpartum Haemorrhage: Prevention and Treatment." *Expert Review of Hematology* 9 (11): 1043–61. <https://doi.org/10.1080/17474086.2016.1245135>.
 - Sosa-Stanley, Jessica N., and Diana C. Peterson.

2018. *Anatomy, Abdomen and Pelvis, Uterus. StatPearls.*

- Vallera, Cristianna, Lynn O Choi, Catherine M Cha, and Richard W Hong. 2017. "Uterotonic Medications: Oxytocin, Methylergonovine, Carboprost, Misoprostol." *Anesthesiology Clinics* 35 (2): 207–19. <https://doi.org/10.1016/j.anclin.2017.01.007>.
- Young, Roger C. 2007. "Myocytes, Myometrium, and Uterine Contractions." In *Annals of the New York Academy of Sciences*, 1101:72–84. Blackwell Publishing Inc. <https://doi.org/10.1196/annals.1389.038>.
- Young, Roger Charles. 2018. "The Uterine Pacemaker of Labor." *Best Practice and Research: Clinical Obstetrics and Gynaecology*. Bailliere Tindall Ltd. <https://doi.org/10.1016/j.bpobgyn.2018.04.002>.