VIA MEDICA

ORIGINAL PAPER / OBSTETRICS

Ginekologia Polska
2022, vol. 93, no. 9, 742–749

ISSN 0017–0011, e-ISSN 2543–6767

DOI 10.5603/GP.a2021.0178

Twin anaemia polycythaemia sequence: a complicated target for prenatal diagnosis, a current state of knowledge

Martin Alfoldi, Ivana Kunochová, Martin Gábor, Vladimír Ferianec

Medical Facutly of Comenius University, Bratislava, Slovakia

ABSTRACT

Objectives: Processing of available information on TAPS with a focus on the evaluation of the most sensitive and most specific prenatal diagnostic test.

Material and methods: Retrospective analysis of available publications on TAPS with their meta-analytical processing through available electronic medical databases. Evaluation of the most sensitive and specific prenatal diagnostic test with graphical processing of sensitivity and specificity values depending on the TAPS diagnostic criteria used.

Results: In total, we found 165 available articles, the oldest from 2007 and the most recent from 2020. Based on the available articles, we evaluated the determination of MCA-PSV with a sensitivity of 83% and a specificity of up to 100% for the currently generally accepted diagnostic criterion TAPS — Delta MCA-PSV > 0.5MoM as the most sensitive and specific method of prenatal diagnosis.

Conclusions: The serial determination of MCA-PSV represents the most sensitive and specific prenatal diagnostic test to date (2020) based on available knowledge. Serial measurement of the MCA-PSV since gestational week 20 every two weeks until delivery represents a potential TAPS screening test for all monochorionic pregnancies. The late, or postnatal diagnosis of TAPS can have serious consequences in the form of intrauterine death of the foetus(es) and increased perinatal mortality and morbidity.

Key words: TTTS (Twin-twin Transfusion Syndrome); TAPS (Twin Anaemia Polycythaemia Sequence); MCA-PSV (Middle Cerebral Artery Peak Systolic Velocity); sensitivity; specificity

Ginekologia Polska 2022; 93, 9: 742–749

INTRODUCTION

The presence of a single placenta, together with the presence of a variable number of interfetal vascular connections of various diameters, provides a basic structural substrate for the development of many intrauterine pathologies typical of monochorionic pregnancy [1]. The angioarchitecture of the monochorionic placenta and the size of the shunting blood volume are the essential determinant of clinical manifestations and possible morphological changes in the affected foetuses [2].

Histopathological examinations of human monochorionic placentas showed three types of vascular connections that differ in their lumens, the type of vessels connected, the size and direction of the shunting blood volume. These three types are arterioarterial (AA), venovenous (VV), and arteriovenous (AV) anastomoses. AA and VV anastomoses are located on the chorionic plate's surface and are bidirectional in terms of blood flow. AV anastomoses are located deep in the placental tissue and are unidirectional [3–6].

TAPS (Twin Anaemia Polycythaemia Sequence), in contrast to TTTS (Twin-twin Transfusion Syndrome), which has been known as a syndromological unit since the 19th century, represents a relatively new syndrome described for the first time in 2007 by Lopriore et al. [7–11]. The main pathophysiological principle of both conditions is the presence of unequal blood distribution between the two foetuses with the formation of a donor-recipient circuit [1, 12, 13]. Compared to TAPS, TTTS is characterized by the shunting of a larger amount of blood, which in addition to changes in the concentration of haemoglobin, is also reflected in changes

Corresponding author:
Vladimir Ferianec
2nd Department of Obstetrics and Gynaecology Faculty of Medicine Comenius University and University Hospital, 4 Ružinovská St, 821 01 Bratislava, Slovakia
e-mail: ferianec@gmail.com

Received: 29.04.2021 Accepted: 19.07.2021 Early publication date: 5.11.2021

in the amniotic fluid volume. It is the change in amniotic fluid volume that represents the basic morphological difference between TTTS and TAPS. In TTTS, imbalanced blood flow occurs through AV anastomoses in the simultaneous absence of AA anastomoses, which, according to the latest findings, represents a protective factor before its development. In the case of monochorionic placentas examined in pregnancies not complicated by TTTS, the presence of AA anastomoses was demonstrated in up to 90%, while in the case of TTTS only 20–25% [6, 7, 14]. Placental preparations in TAPS are characterized by only a few minuscule AV anastomoses in the absence of AA anastomoses. The absence of AA anastomoses is not a prerequisite for the development of TAPS, as there have been described cases where the presence of AA anastomoses has been demonstrated [15–18]. Based on several TAPS cases treated with intrauterine transfusions, it was possible to calculate the approximate amount of shunting blood via AV anastomoses, which was determined to be 5–15 mL/24h [7, 19, 20]. Such a small amount of shunting blood provides sufficient time for haemodynamic compensation in both foetuses and prevents the development of differences in the amniotic fluid volume (Fig. 1) [21, 22].

TAPS occurs in two forms: spontaneous (primary) and post-ablative (secondary) in terms of aetiopathogenesis. The spontaneous (primary) form is rarer and occurs without prior intrauterine surgery on placental vessels. In contrast, the post-ablative form, more frequent, occurs iatrogenically based on foetoscopic laser ablation treatment with occlusion of AV anastomoses in TTTS cases. The development of the post-ablative form of TAPS is therefore interpreted as a complication of intrauterine treatment of TTTS when several minuscule AV anastomoses persist [23–25].

The incidence of the post-ablative form of TAPS is very different and, according to most authors, is around 13%, while the incidence of the spontaneous form of TAPS is relatively constant and is about 3–5% [23].

Diagnosis is possible based on several direct and indirect diagnostic methods, prenatally and postnatally. Postnatally, the diagnosis of TAPS can be made by determining the concentration of haemoglobin, haematocrit, and the number of reticulocytes or their ratio in both foetuses. There are different opinions among the authors on the values of blood count in foetuses, confirming TAPS diagnosis. Lewi's working group defined TAPS as the haemoglobin concentration in the anaemic foetus < 111g/L with the concurrent haemoglobin value in the polycythaemic foetus > 200 g/L. The disadvantage of such strictly determined cut-off values of the red blood component is that they do not include the dynamics of foetal haemoglobin concentration in relation to particular gestational weeks [26–29]. Slaghekke et al., considered the above and tried to correlate the values to gestational weeks. They defined TAPS as anaemia in the donor, with a haemoglobin value < 5 percentile for a given gestational week with concomitant polycythaemia in the recipient, defined as a haematocrit value > 65% [2]. Eurofoetus criteria define TAPS based on the difference in haemoglobin values between the donor and recipient > 80 g/L [2]. The disadvantage of a solitary criterion such determined lies in the fact that in monochorionic pregnancies, even in the absence of TAPS, relatively significant differences in haemoglobin levels can occur in both foetuses due to the development of acute intrapartum TTTS or acute foetoplacental shunting after the birth of the first foetus. Therefore, most authors point to the possibility of using different re-

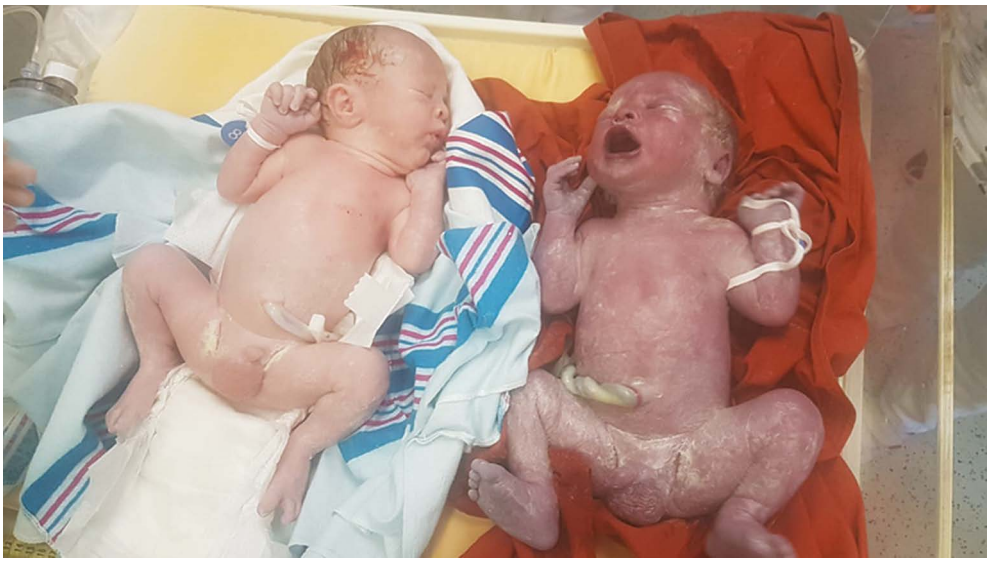

Figure 1. Monochorionic twins complicated by TAPS, gestational week 36, donor twin — anemia, recipient twin — polycythemia

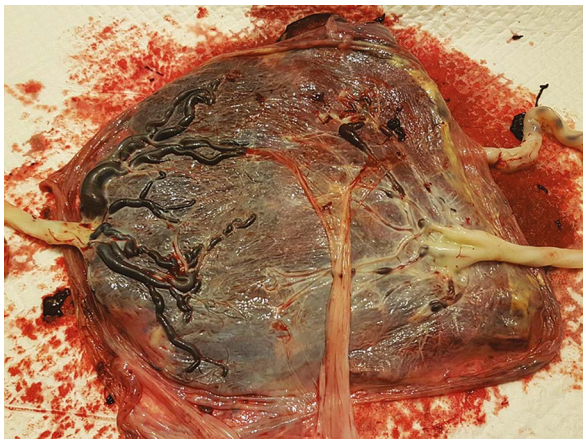

Figure 2. Fetal side of the monochorionic placenta complicated by TAPS — hyperemic vessels belong to recipient twin, collapsed to donor twin

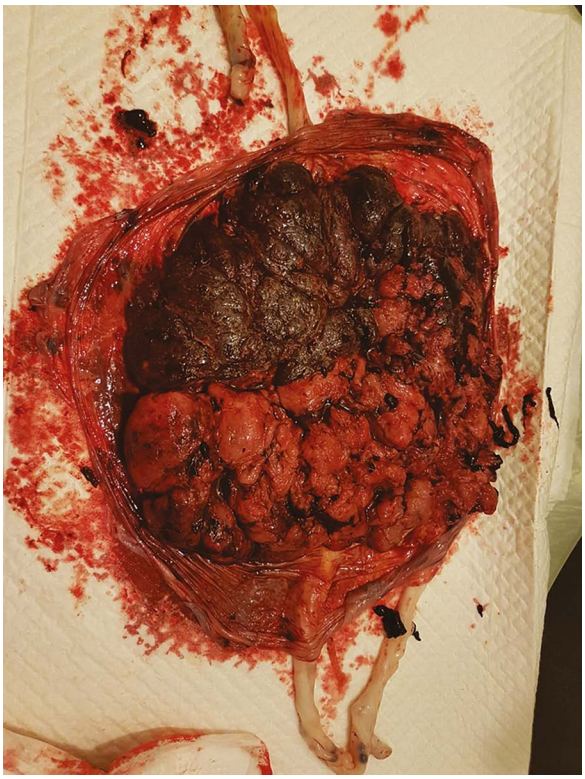

Figure 3. Maternal side of the monochorionic placenta complicated by TAPS — hyperemic part belongs to recipient twin, anaemic to donor twin

ticulocyte counts in both foetuses, representing a general marker of physiologically or pathologically enhanced haematopoiesis. Slaghekke et al., report a difference in reticulocyte count > 3.5% for monochorionic twins as diagnostic for TAPS. The ratio can also express significant changes in reticulocyte levels typical of TAPS. The value of the mutual ratio of the number of donor-recipient reticulocytes > 1.7 is pathognomonic for the diagnosis of TAPS [30, 31].

The latter method, which is rarely used in most clinical workplaces, is a histopathological examination of the placenta, accompanied by injection studies and visualization of particular types of vascular connections. Strict criteria and histopathological characteristics of "physiological" monochorionic placentas do not currently exist, but TAPS is characterized by a small number of AV anastomoses in the concurrent absence of AA anastomoses. The absence of AA anastomoses in monochorionic placentas is frequent in TAPS, but not pathognomonic, since TAPS cases with AA anastomoses have been reported (Fig. 2, 3) [15, 32–34].

In the case of prenatal diagnosis of TAPS, ultrasound examination is the only practically available modality. Ultrasound examination of monochorionic twins suspected of the presence of TAPS evaluates morphological as well as flow criteria. Since TAPS represents a relatively new syndromological unit, its ultrasound criteria are not yet completely uniform. In general, from a morphological ultrasound finding, the absence of amniotic fluid discordances between foetuses is essential for the diagnosis of TAPS. Its presence certainly rules out the diagnosis of TTTS and suggests the presence of TAPS [35, 36].

The available literature also describes the so-called " minor" ultrasound, morphological criteria such as the image of placental dichotomy (demarcation of placental tissue with hyperechogenic, thicker, hydropic tissue on donor side and physiological finding on recipient side) [37] and the image of hepatic parenchyma of starry sky appearance, "starry sky liver" (hypoechogenic hepatic parenchyma of the recipient with hyperechogenic dilated portal venules) [38]. Their more extensive application in prenatal diagnosis has yet to be supported by enough studies.

However, measuring the peak systolic flow velocity in the cerebral artery in both foetuses, in the Anglo-Saxon literature referred to as middle cerebral artery peak systolic velocity (MCA-PSV), is crucial for the diagnosis of TAPS and, in part, the quantification of the severity of the disorder. Changes in MCA-PSV reflect changes in foetal blood viscosity that is predominantly affected by foetal haematocrit. MCA-PSV values expressed in multiples of medians (MoM) for a given gestational week represent an indirect reflection of the number of foetal erythrocytes in the circulation of both foetuses. MCA-PSV values > 1.5 MoM are diagnostic for the presence of anaemia, while values < 0.8 MoM are diagnostic for the presence of polycythaemia in the foetus in cases of single-foetal pregnancies. The value of the difference in MCA-PSV between the donor and the recipient is more critical for TAPS diagnosis than their absolute values in individual foetuses (Tab. 1) [39–41].

Despite the relatively wide application of MCA-PSV in the diagnosis of foetal anaemia in single-foetal pregnancies, the sensitivity and specificity of the above criteria in mul-

Table 1. TAPS stages - diagnostic criteria — 2019 [53]

Stages	Diagnostic criteria
1.	Delta MCA-PSV > 0.5 MoM, with no signs of haemodynamic risk to the foetuses
2.	Delta MCA-PSV > 0.7 MoM, with no signs of haemodynamic risk to the foetuses
3.	Stage 1 or 2 with signs of haemodynamic risk to the donor*
4.	Signs of hydrops in the donor
5.	Intrauterine demise of one or both foetuses preceded by TAPS

*Absence or reversibility of end-diastolic flow in the umbilical artery, pulsatile flow in the umbilical vein, and/or increased pulsatile index or reverse flow in the ductus venosus. MCA-PSV — Middle Cerebral Artery Peak Systolic Velocity, MoM — Multiple of Medians, TAPS — Twin Anaemia Polycythaemia Sequence

ti-foetal pregnancies are still being investigated. The validity and the interpretability of the measurements can be significantly biased, especially in the third trimester of pregnancy, due to the foetuses' spatial presentation. TAPS, analogously to TTTS, can be stratified into several stages based on the degree of severity (Tab. 1) [27].

Therapeutic options for confirmed TAPS are diverse and include observation, induction of labour, intrauterine transfusion, laser, ablation therapy, and controlled selective feticide. The choice of treatment is strictly individual, with the dominant factors being the gestational age at the time of diagnosis and the severity of the disorder. Observation and monitoring are appropriate in late gestational weeks and a milder form of the disorder with relatively good haemodynamic compensation. Cases of post-ablative form of TAPS with spontaneous improvement have been reported. According to the currently available literature, the mortality rate associated with the individual therapeutic modalities is approximately the same. However, observational or expectant management is associated with higher neonatal and perinatal morbidity compared to intrauterine transfusion or laser ablation treatment [42–45].

Administration of intrauterine transfusions is a suitable option for the manifestation of the disorder in the early gestational weeks, as it allows temporary improvement in the condition of the anaemic foetus, delay of premature birth, and prolongation of pregnancy. However, intrauterine transfusions are not a causal treatment, and despite a temporary correction of anaemia in the donor, most cases of TAPS recur within one week. In addition, repeated administration deteriorates the condition of the polycythaemic foetus [46–48]. In the case of transfusion therapy, some authors prefer intraperitoneal to intraumbilical administration, as erythrocytes persist longer in the abdominal cavity with slower release and less overload of the recipient circulation [49].

Laser ablation therapy is the only causal treatment for TAPS, but sporadically presented cases indicate different results. Performing fetoscopic laser ablation in the case of TAPS is more technically demanding compared to ablation in the case of TTTS, as there is no intrauterine working window in the form of polyhydramnios and vascular connectors in the form of AV anastomoses are minuscule, deeply located and difficult to visualize [28].

Assessing short-term and long-term mortality and morbidity in TAPS cases is challenging, as many cases remain prenatally undiagnosed. Slaghekke et al., report the results of a randomized controlled trial of 19 TAPS cases (38 foetuses). The incidence of neonatal mortality and morbidity was comparable in both groups — TAPS 3% (1/38) *vs.* control group 1% (1/76), TAPS (24% 9/38) *vs.* control group (28% 21/76). Severe brain damage occurred in one foetus in the TAPS group (5%), and a similar result was reported in the control group (2%). In the TAPS group, transfusion was reported in 80% of donors (15/19) and partial exchange transfusion in 68% of recipients (13/19) [2]. Due to the insufficient size of the groups of children from pregnancies complicated by TAPS, long-term mortality and morbidity are still the subject of research with preliminary results showing that approximately 9% of foetuses are affected by long-term developmental impairment [50]. Han et al., published a retrospective comparative study of preterm (24–27 gestational week) foetuses from monochorionic pregnancies where they recorded an incidence of spontaneous TAPS in 6.4% based on the postnatal determination of haematocrit in foetuses. Foetuses from TAPS-affected pregnancies had a lower gestational age at delivery, with perinatal mortality and morbidity not different from the control group. The incidence of a severe cerebral lesion in neonatal age and persistent sensorimotor deficit at two years of age was not statistically significantly different in the TAPS and the control group [51]. One Dutch study compared the incidence of neurodevelopmental disorders between donors and recipients in pregnancies complicated by spontaneous TAPS occurrence. According to published findings, donors have a 4-fold higher risk of neurodevelopmental disorders, cognitive delay, and a high rate of deafness [52].

MATERIAL AND METHODS

Based on the available literature (04/2020) using electronic research databases (PubMed, Google Scholar, Dyna Med, Web of Science, Scopus), we created a meta-analytical review of up-to-date knowledge on TAPS with a focus on current options for early detection and subsequent effective management. We analysed the available prenatal diagnosis modalities with an emphasis on the effective TAPS screening in the management of monochorionic pregnancies. The quality of MCA-PSV as a main diagnostic modality pub-

Table 2. Sensitivity and specificity of MCA-PSV in the diagnosis of TAPS

Study	Defined criteria	Sensitivity (95% CI)	Specificity (95% CI)	Positive predictive value (95% CI)	Negative predictive value (95% CI)
Slaghekke et al. 2015 [55]	MCA-PSV ≥ 1.5 MoM — donor MCA-PSV ≥ 1.0 MoM — recipient	**94%** (85–98%) **97%** (87–99%)	**74%** (62–83%) **96%** (89–99%)	**76%** (65–85%) **93%** (81–97%)	**94%** (83–98%) **99%** (93–100%)
Veujoz et al. 2015 [59]	MCA-PSV > 1.5 MoM — donor and simultaneously MCA-PSV < 1.0 MoM	**71%** (29–96%)	**50%** (1–99%)	**83%**	**33%**
Tollenaar et al. 2019 [53]	MCA-PSV > 1.5 MoM — donor and simultaneously MCA-PSV < 1.0 MoM MoM — recipient Delta MCA-PSV > 0.5 MoM	**46%** (30–62%) **83%** (67–92%)	**100%** (92–100%) **100%** (92–100%)	**100%** (81–100%) **100%** (88–100%)	**70%** (58–80%) **88%** (77–94%)

CI — Confidence Interval; MCA-PSV — Middle Cerebral Artery Peak Systolic Velocity; MoM — Multiple of Medians

lished in defined papers was graphically recorded using a table depending on the established diagnostic criteria of TAPS in individual studies (Tab. 2). Data on sensitivity and specificity with various MCA-PSV cut-off values were mostly calculated by use of standard binominal 2 x 2 tables with a determination of 95% Confidence Interval (95% CI) based on the Wilson interval method. The nature of the continuous variables was corrected using Mann-Whitney U-test. However, the exact methods are stated in the original papers cited.

RESULTS

After entering key words (Twin Anaemia Polycythaemia Sequence), we obtained 165 articles, the oldest from 2007 and the most recent from 2020. Due to a low incidence of TAPS, currently the only described methodology in prenatal diagnosis is the determination or secondary comparison of given MCS-PSV values in individual foetuses. Some papers describe morphological organ changes in individual foetuses but without exact determination of sensitivity and specificity values due to an insufficiently large cohort regarding statistical evaluation. Based on the available articles, we evaluated the determination of MCA-PSV with a sensitivity of 83% and a specificity of up to 100% for the currently generally accepted diagnostic criterion TAPS — Delta MCA-PSV > 0.5MoM as the most sensitive and specific method of prenatal diagnosis. Data on sensitivity 83% and specificity 100% with a cut-off value – delta MCA-PSV > 0.5 was for the first time determined in paper published by Tollenaar et al., in 2019 (Tab. 2) [53].

DISCUSSION

TAPS, as a phenomenon known for almost 13 years, is still an underestimated complication of monochorionic pregnancies. The absence of unambiguous morphological markers during the ultrasonographic examination, combined with a relatively low incidence, is the leading cause of low disease detection [50].

Even though some papers report the occurrence of some so-called "minor" ultrasonographic morphological markers, the frequency of their presence has not yet been clearly assessed through large, randomized studies. Tollenar's working group monitored the prevalence of minor markers in 91 cases of monochorionic pregnancies complicated by the occurrence of a spontaneous and post-ablative form of TAPS, recording the prevalence of placental dichotomy in 44% and a so-called "starr sky liver" in 66%. Based on the above, these markers can be considered a complementary and active search for them should be included in a comprehensive second-trimester morphological examination of monochorionic pregnancies [8, 20].

Based on published studies, the only non-invasive technique enabling early, prenatal diagnosis of TAPS is serial examinations of MCA-PSV of individual foetuses at regular intervals [18, 21]. The sensitivity and specificity of this examination in cases of monochorionic pregnancies complicated by the occurrence of TAPS depends on the set diagnostic criteria (Tab. 2) as it was found that cut-off values for the detection of foetal anaemia in single-foetal pregnancies (MCA-PSV > 1.5 MoM) may not be of diagnostic value in TAPS cases. Originally applied criteria defined for the diagnosis of anaemia or polycythaemia in single-foetal pregnancies showed reduced sensitivity and specificity in TAPS diagnosis. Currently, the difference in MCA-PSV in both foetuses > 0.5 MoM is considered diagnostic for TAPS (Delta MCA-PSV > 0.5 MoM) [53].

Despite the documented sensitivity, specificity, non-invasiveness, safety, and cost-effectiveness of MCA-PSV, no clear recommendations are currently issued for its widespread use as a potential screening method for TAPS in the diagnosis of monochorionic pregnancies.

In the United States, according to the recommendations of the Society for Maternal-Fetal Medicine (SMFM), routine serial measurement of MCA-PSV in monochorionic pregnancies is not suitable, as the Society declares that despite early detection of potential TAPS, perinatal mortality and foetal morbidity are not reduced. The Society admits measurement in TTTS cases after ablation treatment where there is a high probability of TAPS prevalence

Table 3. Therapeutic algorithm of TAPS proposed by Tollenaar et al. [28]

Treatment modality	Indication criterion
Expectant management	TAPS Stage 1 regardless of the gestational week TAPS Stage 2 without signs of progression in the period > 28th gestational week
Laser bichorionization of placenta	TAPS Stage ≥ 2 and gestational age < 28 weeks
Intrauterine blood transfusion with laser ablation treatment	TAPS Stage ≥ 3 or Stage 2 with signs of progression in the period between 28–32 gestational weeks
Induction of labour	TAPS Stage ≥ 3 or Stage 2 with signs of progression in the period after the end of the 32nd gestational week

TAPS — Twin Anaemia Polycythaemia Sequence

but does not specify the time intervals between individual examinations [8].

NICE (National Institute for Health and Care Excellence) similarly recommends serial measurements only in the presence of pathology and likewise does not specify the time intervals between individual examinations [57].

ISUOG (The International Society of Ultrasound in Obstetrics & Gynaecology) recommends serial determination of MCA-PSV in all monochorionic pregnancies from gestational week 20 with two-week intervals until delivery [58].

Despite incoherent recommendations, many of which have the character of a so-called "expert opinion", part of the authors in the clinics of maternal and foetal medicine, especially in the United States of America, sets the MCA-PSV from gestational week 16 despite technical difficulties in measuring and difficulty to interpret results [50].

Since serial measurement of MCA-PSV remains the only diagnostic modality for early diagnosis of TAPS to date, according to some authors, its widespread use is suitable for early detection and possible therapeutic intervention in verifying this complication [50]. The above view is also supported by Hill and colleagues' work, which states that expectant management is associated with poorer perinatal outcomes than laser ablation therapy and administration of intrauterine transfusions.

Based on meta-analytical evaluation of the available literature, the authors of the publication are inclined to the opinion supporting the importance of determining MCA-PSV in monochorionic pregnancies. The serial assessments of MCA-PSV allow for the early detection of the disorder and provides sufficient information to patients with the possibility of the next therapeutic procedure's initial planning. According to the authors, serial MCA-PSV measurements should be performed in all monochorionic pregnancies as a TAPS screening test from gestational week 20 every two weeks until delivery.

Many published case studies confirm the need for serial measurement of MCA-PSV to determine the prenatal diagnosis of TAPS [1, 6].

The modality of treatment and the method of its application depend mainly on the severity of the condition (TAPS Stage 1–5), the gestational age of the foetuses, and the patient's preferences. In general, with decreasing gestational age and increasing severity of the disorder, a significant shift from conservative management to invasive procedures regarding laser bichorionization of the placenta can be observed. Minor forms of TAPS diagnosed in advanced gestational age are usually managed conservatively. An indicative chronological arrangement of therapeutic options in the case of pregnancies complicated by the development of TAPS was developed and published by Tollenaar et al. [28], in 2016 (Tab. 3).

Conflict of interest

All authors declare no conflict of interest.

REFERENCES

1. Hack KEA, Nikkels PGJ, Koopman-Esseboom C, et al. Placental characteristics of monochorionic diamniotic twin pregnancies in relation to perinatal outcome. Placenta. 2008; 29(11): 976–981, doi: 10.1016/j.placenta.2008.08.019, indexed in Pubmed: 18835495.
2. Slaghekke F, Kist WJ, Oepkes D, et al. TAPS and TOPS: two distinct forms of feto-fetal transfusion in monochorionic twins. Z Geburtshilfe Neonatol. 2009; 213(6): 248–254, doi: 10.1055/s-0029-1241884, indexed in Pubmed: 20099211.
3. Shanahan MA, Bebbington MW. Placental anatomy and function in twin gestations. Obstet Gynecol Clin North Am. 2020; 47(1): 99–116, doi: 10.1016/j.ogc.2019.10.010, indexed in Pubmed: 32008674.
4. Zhao DP, de Villiers SF, Slaghekke F, et al. Prevalence, size, number and localization of vascular anastomoses in monochorionic placentas. Placenta. 2013; 34(7): 589–593, doi: 10.1016/j.placenta.2013.04.005, indexed in Pubmed: 23639577.
5. Lopriore E, Slaghekke F, Middeldorp JM, et al. Accurate and simple evaluation of vascular anastomoses in monochorionic placenta using colored dye. J Vis Exp. 2011(55): e3208, doi: 10.3791/3208, indexed in Pubmed: 21912373.
6. Lewi L, Cannie M, Blickstein I, et al. Placental sharing, birthweight discordance, and vascular anastomoses in monochorionic diamniotic twin placentas. Am J Obstet Gynecol. 2007; 197(6): 587.e1–587.e8, doi: 10.1016/j.ajog.2007.05.009, indexed in Pubmed: 18060944.
7. Lopriore E, Middeldorp JM, Oepkes D, et al. Twin anemia-polycythemia sequence in two monochorionic twin pairs without oligo-polyhydramnios sequence. Placenta. 2007; 28(1): 47–51, doi: 10.1016/j.placenta.2006.01.010, indexed in Pubmed: 16516289.
8. Simpson LL. Society for Maternal-Fetal Medicine. Twin-twin transfusion syndrome. Am J Obstet Gynecol. 2013; 208(1): 3–18, doi: 10.1016/j.ajog.2012.10.880, indexed in Pubmed: 23200164.
9. Mackie FL, Hall MJ, Morris RK, et al. Early prognostic factors of outcomes in monochorionic twin pregnancy: systematic review and meta-analysis. Am J Obstet Gynecol. 2018; 219(5): 436–446, doi: 10.1016/j.ajog.2018.05.008, indexed in Pubmed: 29763608.
10. Stagnati V, Zanardini C, Fichera A, et al. Early prediction of twin-to-twin transfusion syndrome: systematic review and meta-analysis. Ultrasound

Obstet Gynecol. 2017; 49(5): 573–582, doi: 10.1002/uog.15989, indexed in Pubmed: 27270878.
11. Sueters M, Middeldorp JM, Lopriore E, et al. Timely diagnosis of twin-to-twin transfusion syndrome in monochorionic twin pregnancies by biweekly sonography combined with patient instruction to report onset of symptoms. Ultrasound Obstet Gynecol. 2006; 28(5): 659–664, doi: 10.1002/uog.3819, indexed in Pubmed: 16969785.
12. Wohlmuth C, Boudreaux D, Moise KJ, et al. Cardiac pathophysiology in twin-twin transfusion syndrome: new insights into its evolution. Ultrasound Obstet Gynecol. 2018; 51(3): 341–348, doi: 10.1002/uog.17480, indexed in Pubmed: 28370497.
13. Moaddab A, Nassr AA, Espinoza J, et al. Twin anemia polycythemia sequence: a single center experience and literature review. Eur J Obstet Gynecol Reprod Biol. 2016; 205: 158–164, doi: 10.1016/j.ejogrb.2016.08.033, indexed in Pubmed: 27597647.
14. Tollenaar LSA, Slaghekke F, van Klink JMM, et al. Twin-twin transfusion syndrome with anemia-polycythemia: prevalence, characteristics, and outcome. J Clin Med. 2019; 8(8), doi: 10.3390/jcm8081129, indexed in Pubmed: 31366031.
15. Lopriore E, Deprest J, Slaghekke F, et al. Placental characteristics in monochorionic twins with and without twin anemia-polycythemia sequence. Obstet Gynecol. 2008; 112(4): 753–758, doi: 10.1097/AOG.0b013e318187e1ff, indexed in Pubmed: 18827116.
16. Bae JY, Oh JJu, Hong SY. Prenatal diagnosis of spontaneous twin anemia-polycythemia sequence and postnatal examination of placental vascular anastomoses. Obstet Gynecol Sci. 2016; 59(6): 539–543, doi: 10.5468/ogs.2016.59.6.539, indexed in Pubmed: 27896259.
17. Zhao D, Villiers Sde, Oepkes D, et al. Monochorionic twin placentas: Injection technique and analysis. Diagnóstico Prenatal. 2014; 25(2): 35–42, doi: 10.1016/j.diapre.2013.09.001.
18. Couck I, Lewi L. The placenta in Twin-to-Twin Transfusion Syndrome and Twin Anemia Polycythemia Sequence. Twin Res Hum Genet. 2016; 19(3): 184–190, doi: 10.1017/thg.2016.29, indexed in Pubmed: 27098457.
19. Gillan J, Malley A, Cooley S, et al. 707: Arteriovenous shunts (AVS) occur in the placenta: unexpected evidence from histological examination. American Journal of Obstetrics and Gynecology. 2014; 210(1): S347–S348, doi: 10.1016/j.ajog.2013.10.740.
20. Diehl W, Hecher K, Zikulnig L, et al. Placental vascular anastomoses visualized during fetoscopic laser surgery in severe mid-trimester twin-twin transfusion syndrome. Placenta. 2001; 22(10): 876–881, doi: 10.1053/plac.2001.0710, indexed in Pubmed: 11718576.
21. Slaghekke F, Lewi L, Middeldorp JM, et al. Residual anastomoses in twin-twin transfusion syndrome after laser: the Solomon randomized trial. Am J Obstet Gynecol. 2014; 211(3): 285.e1–285.e7, doi: 10.1016/j.ajog.2014.05.012, indexed in Pubmed: 24813598.
22. Favre R, Koch A, Weingertner AS, et al. Vascular pattern in monochorionic placentas with spontaneous TAPS and TTTS with residual anastomoses after laser: a case-control study. Prenat Diagn. 2013; 33(10): 979–982, doi: 10.1002/pd.4177, indexed in Pubmed: 23744723.
23. Robyr R, Lewi L, Salomon LJ, et al. Prevalence and management of late fetal complications following successful selective laser coagulation of chorionic plate anastomoses in twin-to-twin transfusion syndrome. Am J Obstet Gynecol. 2006; 194(3): 796–803, doi: 10.1016/j.ajog.2005.08.069, indexed in Pubmed: 16522415.
24. Weingertner AS, Kohler A, Kohler M, et al. Clinical and placental characteristics in four new cases of twin anemia-polycythemia sequence. Ultrasound Obstet Gynecol. 2010; 35(4): 490–494, doi: 10.1002/uog.7508, indexed in Pubmed: 20069657.
25. Kirbas A, Celen S, Caglar T, et al. Antenatal management of twin anemia-polycythemia sequence. Medicine Science | International Medical Journal. 2018; 7(3): 709–712, doi: 10.5455/medscience.2018.07.8830.
26. Jopling J, Henry E, Wiedmeier SE, et al. Reference ranges for hematocrit and blood hemoglobin concentration during the neonatal period: data from a multihospital health care system. Pediatrics. 2009; 123(2): e333–e337, doi: 10.1542/peds.2008-2654, indexed in Pubmed: 19171584.
27. Slaghekke F, Kist WJ, Oepkes D, et al. Twin anemia-polycythemia sequence: diagnostic criteria, classification, perinatal management and outcome. Fetal Diagn Ther. 2010; 27(4): 181–190, doi: 10.1159/000304512, indexed in Pubmed: 20339296.
28. Tollenaar LSA, Slaghekke F, Middeldorp JM, et al. Twin Anemia Polycythemia Sequence: current views on pathogenesis, diagnostic criteria, perinatal management, and outcome. Twin Res Hum Genet. 2016; 19(3): 222–233, doi: 10.1017/thg.2016.18, indexed in Pubmed: 27068715.
29. Liu B, Kalafat E, Bhide A, et al. Performance of antenatal diagnostic criteria of Twin-Anemia-Polycythemia Sequence. J Clin Med. 2020; 9(9), doi: 10.3390/jcm9092754, indexed in Pubmed: 32858863.
30. Visser GL, Tollenaar LSA, Bekker V, et al. Leukocyte counts and other hematological values in Twin-Twin Transfusion Syndrome and Twin Anemia-Polycythemia Sequence. Fetal Diagn Ther. 2020; 47(2): 123–128, doi: 10.1159/000500859, indexed in Pubmed: 31261154.
31. Verbeek L, Slaghekke F, Sueters M, et al. Hematological disorders at birth in complicated monochorionic twins. Expert Rev Hematol. 2017; 10(6): 525–532, doi: 10.1080/17474086.2017.1324290, indexed in Pubmed: 28460542.
32. Fitzgerald B. Histopathological examination of the placenta in twin pregnancies. APMIS. 2018; 126(7): 626–637, doi: 10.1111/apm.12829, indexed in Pubmed: 30129131.
33. Emery SP, Nguyen L, Parks WT. Histological appearance of placental solomonization in the treatment of Twin-Twin Transfusion Syndrome. AJP Rep. 2016; 6(2): e165–e169, doi: 10.1055/s-0036-1582449, indexed in Pubmed: 27127717.
34. Zhao D, Tollenaar LSA, Slaghekke F, et al. Evaluation of color difference in placenta with Twin Anemia Polycythemia Sequence. J Vis Exp. 2020(160), doi: 10.3791/61312, indexed in Pubmed: 32628164.
35. Fishel-Bartal M, Weisz B, Mazaki-Tovi S, et al. Can middle cerebral artery peak systolic velocity predict polycythemia in monochorionic-diamniotic twins? Evidence from a prospective cohort study. Ultrasound Obstet Gynecol. 2016; 48(4): 470–475, doi: 10.1002/uog.15838, indexed in Pubmed: 26663574.
36. Gucciardo L, Lewi L, Vaast P, et al. Twin anemia polycythemia sequence from a prenatal perspective. Prenat Diagn. 2010; 30(5): 438–442, doi: 10.1002/pd.2491, indexed in Pubmed: 20373492.
37. Kusanovic J, Romero R, Gotsch F, et al. Discordant placental echogenicity: a novel sign of impaired placental perfusion in twin-twin transfusion syndrome? J Matern Fetal Neonatal Med . 2009; 23(1): 013–6, doi: 10.1080/14767050903005873, indexed in Pubmed: 19626497.
38. Soundararajan LP, Howe DT. Starry sky liver in twin anemia-polycythemia sequence. Ultrasound Obstet Gynecol. 2014; 43(5): 597–599, doi: 10.1002/uog.13276, indexed in Pubmed: 24339130.
39. Brock CO, Bergh EP, Moise KJ, et al. Middle cerebral artery Doppler velocimetry for the diagnosis of Twin Anemia Polycythemia Sequence: a systematic review. J Clin Med. 2020; 9(6), doi: 10.3390/jcm9061735, indexed in Pubmed: 32512796.
40. Tavares de Sousa M, Fonseca A, Hecher K. Role of fetal intertwin difference in middle cerebral artery peak systolic velocity in predicting neonatal twin anemia-polycythemia sequence. Ultrasound Obstet Gynecol. 2019; 53(6): 794–797, doi: 10.1002/uog.20116, indexed in Pubmed: 30207009.
41. Khalil A, Gordijn S, Ganzevoort W, et al. Consensus diagnostic criteria and monitoring of twin anemia-polycythemia sequence: Delphi procedure. Ultrasound Obstet Gynecol. 2020; 56(3): 388–394, doi: 10.1002/uog.21882, indexed in Pubmed: 31605505.
42. Hill KM, Masoudian P, Fung-Kee-Fung K, et al. Intrauterine interventions for the treatment of Twin Anemia-Polycythemia Sequence: a systematic review. J Obstet Gynaecol Can. 2019; 41(7): 981–991, doi: 10.1016/j.jogc.2018.04.005, indexed in Pubmed: 31230662.
43. Yarci E, Alyamac Dizdar E, Oncel MY, et al. Successful management of twin anemia/polycythemia sequence by syngeneic partial exchange transfusion. Fetal Diagn Ther. 2014; 36(3): 251–254, doi: 10.1159/000360079, indexed in Pubmed: 25095971.
44. Sananès N, Veujoz M, Severac F, et al. Evaluation of the utility of in utero treatment of Twin Anemia-Polycythemia Sequence. Fetal Diagn Ther. 2015; 38(3): 170–178, doi: 10.1159/000380822, indexed in Pubmed: 25790745.
45. Slaghekke F, Favre R, Peeters SHP, et al. Laser surgery as a management option for twin anemia-polycythemia sequence. Ultrasound Obstet Gynecol. 2014; 44(3): 304–310, doi: 10.1002/uog.13382, indexed in Pubmed: 24706478.
46. Slaghekke F, van Klink JMM, Koopman HM, et al. Neurodevelopmental outcome in twin anemia-polycythemia sequence after laser surgery for twin-twin transfusion syndrome. Ultrasound Obstet Gynecol. 2014; 44(3): 316–321, doi: 10.1002/uog.13387, indexed in Pubmed: 24753027.
47. Genova L, Slaghekke F, Klumper FJ, et al. Management of twin anemia-polycythemia sequence using intrauterine blood transfusion for the donor and partial exchange transfusion for the recipient. Fetal Diagn Ther. 2013; 34(2): 121–126, doi: 10.1159/000346413, indexed in Pubmed: 23713060.

48. Lindenburg ITM, van Kamp IL, Oepkes D. Intrauterine blood transfusion: current indications and associated risks. Fetal Diagn Ther. 2014; 36(4): 263–271, doi: 10.1159/000362812, indexed in Pubmed: 24903741.
49. Herway C, Johnson A, Moise K, et al. Fetal intraperitoneal transfusion for iatrogenic twin anemia-polycythemia sequence after laser therapy. Ultrasound Obstet Gynecol. 2009; 33(5): 592–594, doi: 10.1002/uog.6334, indexed in Pubmed: 19402103.
50. Nicholas L, Fischbein R, Aultman J, et al. Dispelling myths about antenatal TAPS: a call for action for routine MCA-PSV Doppler screening in the United States. J Clin Med. 2019; 8(7), doi: 10.3390/jcm8070977, indexed in Pubmed: 31277521.
51. Han SJ, Lee SMi, Oh S, et al. Short- and long-term outcomes of preterm spontaneous twin anemia-polycythemia sequence. J Perinat Med. 2020 [Epub ahead of print], doi: 10.1515/jpm-2019-0437, indexed in Pubmed: 32229695.
52. Tollenaar LSA, Lopriore E, Slaghekke F, et al. High risk of long-term neurodevelopmental impairment in donor twins with spontaneous twin anemia-polycythemia sequence. Ultrasound Obstet Gynecol. 2020; 55(1): 39–46, doi: 10.1002/uog.20846, indexed in Pubmed: 31432580.
53. Tollenaar LSA, Lopriore E, Middeldorp JM, et al. Improved prediction of twin anemia-polycythemia sequence by delta middle cerebral artery peak systolic velocity: new antenatal classification system. Ultrasound Obstet Gynecol. 2019; 53(6): 788–793, doi: 10.1002/uog.20096, indexed in Pubmed: 30125414.
54. Tollenaar LSA, Lopriore E, Middeldorp JM, et al. Prevalence of placental dichotomy, fetal cardiomegaly and starry-sky liver in twin anemia-polycythemia sequence. Ultrasound Obstet Gynecol. 2020; 56(3): 395–399, doi: 10.1002/uog.21948, indexed in Pubmed: 31856326.
55. Slaghekke F, Pasman S, Veujoz M, et al. Middle cerebral artery peak systolic velocity to predict fetal hemoglobin levels in twin anemia-polycythemia sequence. Ultrasound Obstet Gynecol. 2015; 46(4): 432–436, doi: 10.1002/uog.14925, indexed in Pubmed: 26094734.
56. Oepkes D, Seaward PG, Vandenbussche FP, et al. DIAMOND Study Group. Doppler ultrasonography versus amniocentesis to predict fetal anemia. N Engl J Med. 2006; 355(2): 156–164, doi: 10.1056/NEJMoa052855, indexed in Pubmed: 16837679.
57. National Institute for Health and Care Excellence (UK). Twin and triplet pregnancy. NICE Guideline, No. 137. 2019.
58. Khalil A, Rodgers M, Baschat A, et al. ISUOG Practice Guidelines: role of ultrasound in twin pregnancy. Ultrasound Obstet Gynecol. 2016; 47(2): 247–263, doi: 10.1002/uog.15821, indexed in Pubmed: 26577371.
59. Veujoz M, Sananès N, Severac F, et al. Evaluation of prenatal and postnatal diagnostic criteria for twin anemia-polycythemia sequence. Prenat Diagn. 2015; 35(3): 281–288, doi: 10.1002/pd.4545, indexed in Pubmed: 25484182.