Comparison of Internal Jugular Vein Cross-Section Area During a Russian Tilt-Table Protocol and Microgravity

Jason David; Richard A. Scheuring; Andrew Morgan; Cara Olsen; Ashot Sargsyan; Alexey Grishin

BACKGROUND: To date, we lack U.S. data on the effects of the long-used Russian tilt-table training protocol known as the Russian pre-launch tilt-table training protocol on internal jugular vein cross sectional area (IJV-CSA) in microgravity.

CASE REPORT: A case study of a single healthy male astronaut volunteer was used for this study. The right IJV-CSA was measured using real time ultrasound at set times throughout the Russian pre-launch tilt-table training protocol, a method of physiological preparation for microgravity using tilt-table training. In microgravity, the subject's right IJV-CSA was measured again for comparison. The mean difference from in-flight right IJV-CSA for pre-tilt (0°) was −0.438 cm^2, for −15° was 0.887 cm^2, for −30° was 0.864 cm^2, for +50° was −1.15 cm^2, and for post-tilt (0°) the difference was −0.305 cm^2.

DISCUSSION: The cross-sectional areas of the subject's right IJV-CSA were significantly different between in-flight values and several angles of the Russian tilt-table protocol, except for the 0° measurement. In summary, this case-study represents the first time IJV-CSA has been compared between various angles of a tilt-table training protocol and microgravity in the same astronaut subject. The findings support prior cohort studies studying the same principles. Further investigation is merited; both to better describe the relationship between the cardiovascular effects of tilt-table simulations of microgravity and their correlating in-flight values, and to evaluate and study the Russian tilt-table protocol effects on cardiovascular physiology from a training and preparation perspective.

KEYWORDS: internal jugular vein, cross-sectional area, spaceflight, microgravity, Russian pre-launch tilt-table training protocol, Russian tilt-table, ultrasound.

David J, Scheuring RA, Morgan A, Olsen C, Sargsyan A, Grishin A. *Comparison of internal jugular vein cross-section area during a Russian tilt-table protocol and microgravity*. Aerosp Med Hum Perform. 2021; 92(3):207–211.

Fluid shifting in microgravity is a highly documented and studied phenomenon. A thoracic fluid shift is first experienced in the launch position, with feet above the head relative to Earth's gravity, much like the effects of a tilt-table. However, regarding microgravity, it begins upon reaching weightlessness, with the astronaut often feeling a sensation of head fullness. Physically, the astronaut displays facial edema, volume reduction of the lower extremities, and engorgement of the superficial vascular system.[4] The cardiovascular effects of this fluid shifting have also been studied extensively. Clinical consequences of microgravity-induced fluid shifting include lowering of orthostatic tolerance, often causing reductions in cerebral blood flow and fainting in returning crewmembers.[18] Additionally, cardiovascular deconditioning is found to occur, both in terms of cardiac output and cardiac muscle and vascular smooth muscle loss. Fluid shifting is also thought to be one of the main contributing factors to the development of Space Flight-Associated Neuro-ocular Syndrome (SANS).

Studies involving the simulation of microgravity as pertains to fluid shifting and cardiovascular response have often used techniques such as "dry-immersion" or head-down tilt (HDT) for physiological study. There are numerous studies comparing the effects of HDT to those of actual microgravity. One such study by Hargens and Richardson in 2009 postulated, based on their meta-review of the literature to that point, that fluid shifting contributed to an upper extremity and torso edema in

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This manuscript was received for review in January 2020. It was accepted for publication in December 2020.

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DOI: https://doi.org/10.3357/AMHP.5600.2021

microgravity due to the loss of tissue weight and subsequent interstitial fluid pressure as well as an increase in capillary blood pressure in 1 G which shifted the equilibrium toward increased fluid filtration.[6,8,10] This was found to be consistent with the findings of increased fluid filtration capacity during long-duration HDT by Christ et al.[7]

The effects of HDT on internal jugular vein cross-sectional area (IJV-CSA) are also well documented; in 2008, Kim et al. specifically studied passive leg elevation and the Trendelenburg position, and found both significantly increased the IJV-CSA.[12] Schreiber et al. specifically looked at varying angles of HDT recumbence and their effect on IJV-CSA, and found that the 10° head-down tilt maneuver in healthy volunteers caused an immediate increase in IJV-CSA; however, longer tilts did not cause any further increase, i.e., there was no cumulative effect of the time in tilt.[17] However, a 2018 evaluation of IJV-CSA and volume found increases with progressively steeper angles of HDT, with more prominent filling of the internal jugular vein at the clavicle.[15] These effects were verified by phase-contrast MRI during a 2016 study which supported the findings of increased IJV-CSA during HDT, but also additionally found decreased venous outflow at HDT.[13] This could indicate overall decreased cerebral blood flow during HDT, which may have implications for microgravity-induced hemodynamic changes in the brain and related structures such as the eyes and neck, including the formation of thrombi.

While studies both in microgravity and terrestrial analogs such as HDT have demonstrated that arterial diameter and blood flow velocity do not change significantly during spaceflight due to autoregulation, the fluid shifts encountered in microgravity contribute to jugular vein distention, which may be an indicator of cerebral blood flow congestion.[9,11] One of these studies, by Arbeille et al. in 2001, compared cardiovascular changes induced by exposure to microgravity or HDT with minimal to no countermeasures used in the two comparison groups during short and long-duration spaceflight. Several cardiovascular parameters were measured, including jugular vein cross-sectional area, which may be an indicator of cerebral vascular congestion, as mentioned earlier. The study found that the jugular vein size changes were not similar at all between HDT and spaceflight and attributed this discrepancy to differences between intensity of the forces causing the fluid shift, and overall differences in mechanism. The cephalic vein in HDT is exposed to a 0.1-g gravity toward the top of the head, which probably reduces the venous return and thus the jugular vein enlargement.[1]

An additional study by Beggs et al. in 2016 suggested that, in healthy adults, increased CSF pulsatility was associated with increased IJV-CSA by the cervical region of the neck, independent of age and cardiovascular risk factors, suggesting a biomechanical link between the two.[5] Further investigation was done by Martin et al. by measuring internal jugular venous pressure (IJVP) during 1-g gravity, and at 0 G, 1/6 G, and 1/3 G using parabolic flight. The data suggest that IJVP was elevated significantly during acute exposures to hypo-gravity and was further elevated by maneuvers that increase intrathoracic pressure, such as the Valsalva maneuver. Although a definite conclusion was not drawn, there is again, a possible correlation between these increased central venous pressures, consequent venous congestion, and vision change.[16] Possible countermeasures have also been studied. The use of lower body negative pressure (LBNP) to counteract fluid shifting during HDT at 15° was studied by Watkins et al. in 2017, finding quantitative evidence that LBNP did in fact shift cephalic fluid to the lower body during a tilt-table test, reducing IJV-CSA and intracranial pressure.[19] Regarding the actual comparison between IJV-CSA terrestrially to microgravity, a 2015 study by Arbeille et al. to evaluate changes in major central and peripheral veins over a period of 6 mo in orbit was conducted. Using a volume-capture method using 3D image reconstruction, measurements of the IJV-CSA were taken preflight, day 15 of flight, 4–5.5 mo into the flight, and postflight. IJV-CSA was found to increase by 178 and 225%, respectively, and returned to baseline conditions 4 d after returning to Earth, adding to further evidence of venous blood pooling in the cephalic region.[2]

Finally, a study in 2019 by Marshall-Goebel et al.[14] studied the effects of internal jugular vein flow and morphology during spaceflight as well as lower body negative pressure effects on headward fluid shifts in spaceflight. A prospective cohort of 11 astronauts flying missions aboard the International Space Station were studied. Internal jugular vein measurements from before launch, in flight at 50 and 150 d, and approximately 40 d after landing were acquired in three positions: seated, supine, and 15° head-down tilt. The in-flight measurements were taken both during normal spaceflight conditions and with the use of a lower body negative pressure device. Ultrasound measurements of IJV-CSA, pressure, blood flow, and thrombus formation were analyzed. The study found significant increases in IJV-CSA during spaceflight compared with the seated position but found no significant differences between preflight supine IJV-CSA measurements and the in-flight measurements at day 50 and 150. The study additionally found increases in mean IJV pressures. Most interestingly, findings of stagnant or reverse blood flow were observed in 55% of the subjects, with one crewmember having an occlusive IJV thrombus and a partial IJV thrombus in another upon retrospective analysis, the former occurring 2 mo into travel, which was treated in flight with enoxaparin and apixaban.[3] Regarding the intervention of LBNP, improved IJV blood flow in 59% of sessions during spaceflight was observed.

Given these remarkable findings, urgent further critical inquiry into the physiology of cerebral and internal jugular vein blood flow in spaceflight is apparent. To date, however, there does not seem to be any published literature comparing the effects of several angles of repeat tilt-table testing on IJV-CSA and microgravity IJV-CSA on the same astronaut subject. Furthermore, comparison between Russian tilt-table protocols, which have been used since the late 1970s by the Soviet space program and later Roscosmos, and findings in microgravity has never been conducted in U.S. medical literature before. Therefore, this case study provides an interesting and unique datapoint to the study of internal jugular vein hemodynamics in microgravity, which has potential implications for human brain, eye, and hematologic spaceflight physiology, including SANS and neurocognitive performance in space.

CASE REPORT

A convenience sample of a single healthy male astronaut volunteer was chosen at random by a single examiner for this study. Enrollment and data collection dates are not provided in order to protect the identity of the single subject among a paucity of persons in space in a given year. The data were collected noninvasively during training that the subject would have taken regardless of experiment status. The subject had no history of neck problems, vascular problems, or prior IJV cannulation or procedures. The subject was placed supine/recumbent on a manually controlled tilt table with an inbuilt inclinometer. The right IJV was identified using real time ultrasound [Butterfly iQ (Butterfly Network Inc., Guilford, CT, USA) ultrasound in M-Mode, stored on iPad 5th gen.]. The subject's right IJV-CSA was measured at the same level once initially at 0°, then during two respiratory cycles at inspiration and expiration. The subject was then tilted according to the Roscosmos protocol (see **Table I**). As the subject was tilted, ultrasound measurements of the CSA were gathered and recorded. These measurements were taken 8 d before flight.

Multiple measurements of the CSA were taken at −15°, −30°, and +50°, along with 0° (pre-tilt) and 0° (post-tilt). The average CSA was computed for each angle and compared to the in-flight average using Student's *t*-test. A single measurement taken at −45° is reported but could not be compared statistically due to lack of replication.

Table I. Russian Pre-Launch Tilt-Table Training Protocol and Associated Durations Spent at Each Degree of Tilt from Recumbency (0°).

DEGREES	TIME
0°	Starting position
−15°	1.5 min
+50°	1 min
−15°	1.5 min
+50°	1 min
−30°	2 min
+0°	1 min
−30°	2 min
+50°	1 min
−30°	2 min
+50°	1 min
−45°	1 min
+50°	1 min
−30°	2 min
+50°	1 min
−30°	2 min
+50°	1 min
−30°	2 min
+50°	1 min
−15°	1.5 min
+50°	1 min
−15°	1.5 min
+50°	1 min
0°	Return position

Clear ultrasound images of the subject's right IJV were obtained, with no anatomical or hematologic abnormalities encountered. The mean right IJV-CSA was measured at intermittent points throughout the entire protocol, with mean values noted in **Table II**.

DISCUSSION

Fluid redistribution and blood flow in microgravity are key areas of study for space medicine and physiology, both in respect to SANS and in a general sense. The Marshall-Goebel study demonstrating blood flow stasis in the left IJV in almost half of its subjects, jugular venous thrombosis (both previously unrecognized risks of spaceflight), and comparing positional measurements of IJV-CSA among the astronaut subjects pre, in-, and postflight was a seminal work that leaves room for significant further investigation into vascular and blood flow phenomena in space. This case study was taken from a convenience sample during a recent ISS mission (both preflight preparation for the mission and in flight) and examined different angles of tilt as well as comparing terrestrial and orbital physiology using a long-established Russian training protocol.

The cross-sectional areas were significantly different between in-flight values and several angles of the Roscosmos protocol as mentioned above. Of note, the end-state right IJV-CSA of the protocol at 0° (horizontal) was not significantly different from the in-flight measurements; however, the sample size of this measurement was small ($N = 2$). Furthermore, the 45° angle measurements could not be formally compared because only one measurement was obtained, per protocol.

Given that this case study's data consist of a single subject of opportunity vs. the multiple subjects enjoyed by prior studies, quantitative comparison would violate the assumptions of most statistical analyses. However, a qualitative comparison of our findings is possible. The value of this case study specifically looking at the effects of the Russian pre-launch tilt-table training protocol is highlighted once examined in light of cumulative microgravity IJV-CSA data from other astronauts. The jugular vein cross-sectional area data from the 2001 Arbeille[1] and 2019 Marshall-Goebel[14] studies are of particular use here. As mentioned previously, the 2001 Arbeille et al. study compared cardiovascular changes, including IJV-CSA, in microgravity to an HDT analog, finding significant differences between the pre-HDT and HDT measurements, as well as preflight and in-flight measurements. The study also found the changes in IJV-CSA were not similar in HDT and spaceflight. The 2019 Marshall-Goebel study, also mentioned earlier, found significant differences in IJV-CSA measurements between 15° HDT and the IJV-CSA measurements in space, but found little to no difference between the supine (horizontal) measurements and in-flight measurements. While their study looked at the left internal jugular vein, our case study does lend unique support to their conclusions, mirroring little to no difference between supine and in-flight measurements, but a statistically significant difference at the −15° angle. It should also be noted that orthostatic

Table II. Results of Terrestrial RIJV-CSA Measurements During the Russian Pre-Launch Tilt-Table Training Protocol.

	0° PRE	0° END	−15°	−30°	−45°	+50°
# Measurements Recorded	5	2	3	5	1	5
Mean Value (cm^2)	0.912	1.045	2.237	2.214	2.53	0.2
Discrepancy vs. in flight (cm^2)	−0.438	−0.305	0.8867	0.864	1.18	−1.15
t-statistic (degrees of freedom)	11.570 (4)	5.545 (1)	4.576 (2)	9.005 (4)	--	55.460 (4)
P-value	0.0003	0.1136	0.0446	0.0008	--	<0.0001
95% confidence interval	−0.5431 to -0.3329	−1.004 to 0.3938	0.05297 to 1.720	0.5976 to 1.130	--	−1.208 to −1.092

countermeasures have evolved since 2001. While the subjects of the aforementioned Arbeille study were noted to be using "minimal levels of countermeasure," the conditions are obviously not the exact same to the conditions in the 2019 Marshall-Goebel study, whose countermeasure conditions also reflect that of our subjects.

An additional point of further study is the effects of the Russian pre-launch tilt-table training protocol on physiological training and preparation for long-term exposure to microgravity. The subject underwent the entire protocol (Table I). An interesting future study would be to compare several cardiovascular measures, such as left ventricle end-diastolic volume, stroke volume, cardiac output, ejection fraction, middle cerebral artery flow velocity, and IJV-CSA, on astronaut/cosmonaut subjects who have undergone the Russian pre-launch tilt-table training protocol vs. a group with no intervention. While Roscosmos has used tilt-table preflight microgravity preparation since around 1977–1978, this is not currently followed by NASA and the relative effectiveness of protocols such as this as a physiological preparation technique is a stimulating potential avenue of research for operational space medicine.

This case study had several limitations. First, being a case study of one subject, the generalizability of this study is low. The limited amount of datapoints we were able to gather during the protocol is difficult to draw a conclusion from, suggesting that further investigation into this protocol be pursued. Second, only one IJV was examined in this study and there may be unaccounted for anatomic differences between the subject's right and left IJVs that could affect cross-sectional area measurements. Third, these measurements were collected only at two points in time: 8 d before spaceflight and 30 d into flight. Further changes may have occurred later in the flight, though the Marshall-Goebel study did not demonstrate any significant difference between in-flight day 50 and day 150 measurements of IJV-CSA.[14]

In summary, this single-subject case study represents, to our knowledge, the first time a comparison of internal jugular vein cross-sectional area has been compared between various angles of a tilt-table training protocol and orbital microgravity in the same astronaut subject, and lends support to similar cohort studies studying the same principles. Significant differences were found between the tilt-table angle values and the in-flight values except for the end supine measurements. Thus, further rigorous investigation is merited; both to better describe the relationship between the cardiovascular effects of tilt-table simulations of microgravity and their correlating in-flight values, and to evaluate and study the Russian pre-launch tilt-table training protocol effects on cardiovascular physiology from a training and preparation perspective.

ACKNOWLEDGMENTS

Financial Disclosure Statement: The authors have no competing interests to declare.

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