Incidental Finding Prevalences in 3-Tesla Brain and Spine MRI of Military Pilot Applicants

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INTRODUCTION: Incidental findings in brain and spine MRI are common. In aerospace medicine, pilot selection may be affected by improved sensitivity of modern MRI devices. We investigated the occurrence of medically unfit rates caused by incidental findings in military pilot applicants using a 3-Tesla scanner as compared to the outcomes of a lower field strength 1-Tesla device based on similar screening protocols.

METHODS: A total of 3315 military pilot applicants were assessed by a standardized German Air Force Imaging Screening Protocol and retrospectively subdivided into two cohorts, one of which was assessed by 1-Tesla MRI (2012-2015; $N = 1782$), while in the second cohort (2016-2019; $N = 1808$), a 3-Tesla MRI was used. Cohorts were statistically analyzed relating to three entities of incidental findings: 1) intervertebral disc displacements, 2) intracerebral vessel malformations, and 3) other abnormal findings in the brain.

RESULTS: Pooled prevalences of incidental findings in medically unfit applicants significantly increased by use of 3-Tesla MRI as compared to lower resolution 1-Tesla MRI. Regarding the spine, prevalences more than doubled (1.46 vs. 4.99%; $P < 0.05$) for intervertebral disc displacements. Similarly, prevalences of cerebral vessel malformations as well as other abnormal CNS incidental findings considerably increased by use of 3-Tesla MRI (0.28 vs. 1.67%; $P < 0.05$, and 5.12 vs. 9.80%; $P < 0.05$). Effect sizes and correlations were substantial in all conditions analyzed (Cohen's $d > 0.8$; Pearson's $r > 0.75$).

CONCLUSIONS: Our data suggest a strong dependency of incidental cerebrospinal findings on image resolution and sensitivity of MRI devices used for screening, which is enhanced by refined imaging protocols and followed by increased medical unfit rates in prospective aviators. Adjusted strategies in the assessment of such lesions are needed to redefine their natural history and physiological impact, and to optimize screening protocols for future pilot selection.

KEYWORDS: Incidental findings, MRI screening, 3-Tesla, brain and spine imaging, military pilot applicants, aerospace medicine.

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The demand for trained pilots has been rising continuously over the past decades. Before the COVID-19 pandemic, Boeing expected a demand for more than 800,000 new pilots worldwide and about 150,000 pilots in Europe over the next 20 yr.[33] With this in mind, German Lufthansa has been educating more than 450 candidates per year, with the result of more than 10,000 pilots currently working in the entire Lufthansa Group environment worldwide.[16] Nevertheless, while there is an unprecedented decline in air traffic caused by the current crisis, with devastating effects on the travel industry as a whole, most experts agree that travel will not return to preoutbreak levels prior the end of 2021.[18,28]

Likewise, it can be expected that the military sector will be seeing a number of postpandemic changes as well.[27] Although military aviation is not affected by the travel industry, and although there has always been a strong role for military forces in Air Medical Evacuation, reduced defense salaries and shortages in aircraft construction and delivery may contribute to the decrease of actual needs for newly educated flight personnel. However, independently from the number of staff needed, it has always been common sense that pilots are expected to display an extraordinary level of individual health and professional

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reliability.[8] In fact, it might be hypothesized that, driven by the current awareness of the public, the demand for flight safety and personal integrity may rather have increased than stabilized.

In this context, preventive medicine plays an important role in lowering the occurrence rates of disease, eventually halting the course of disease and averting complications. Military pilots are exposed to challenging and sometimes, depending on the type of aircraft they are flying, rapidly changing professional environments (e.g., hypoxia, high altitude, acceleration, vibration), each affecting individual health and based-on skills. Hence, within aviation medicine, primary risk reduction, individual health prophylaxis, and human performance optimization are the foremost targets of preventive measures in aircrew and cockpit personnel.[11]

In Germany, the Air Force Centre of Aerospace Medicine in Fürstenfeldbruck is responsible for the examination of military flight candidates applying for military service. For over 20 yr now, the department of radiology has been conducting whole-body magnetic resonance imaging (MRI) examinations, as a screening examination for pilot and other applicants of the flying branch. While before 2016 these examinations were performed using a 1-Tesla scanner, we now use a higher field strength 3-Tesla MRI device. This has enabled us to expand and optimize our former screening protocols by incorporating state-of-the-art contemporary technology. In addition to the conventional T1-weighted and fat-suppressed T2-weighted sequences,[25] the German Air Force standard protocol now includes noncontrast vascular MRI and diffusion-weighted images. Medical military pilot assessment involves several departments, including Neurology, Internal Medicine, Ear-Nose and Throat Medicine, Ophthalmology, Orthopedics, and Dentistry.

However, clinical experience reveals that screening results obtained with new technologies might be more challenging than anticipated before, enabling detection of minor lesions that would have never been seen using the former technology. Since flight accident and incident rates have not changed since the introduction of the new 3-Tesla technology, and as general pilot health has remained stable over the observation period covered by this study, the clinical meaning or relevance of these incidental findings for the individual aviator are unclear.[1,38]

In this study, we address three incidental neuroradiological findings frequently seen at the German Air Force Centre of Aerospace Medicine: 1) intervertebral disc displacements; 2) malformations of cerebral vessels like nonruptured cerebral aneurysms and congenital malformations of cerebral vessels; and 3) other abnormal findings on diagnostic imaging of the central nervous system. Findings are analyzed and discussed in the context of technical innovation, its advantages and drawbacks, and with respect to flight safety considerations.

METHODS

Screening Protocol

The German Air Force Imaging Screening Protocol (GAF-ISP) is designed to detect and validate topographic pathologies in first-time military applicants to minimize possible human factor-related hazards to flight safety.[4] Supplementary to X-ray and CT-imaging, MRI was introduced in 2000 as a 1T device, and expanded in 2016 to a 3T device. For brain scans, enhanced imaging with multiplane T2 weighted and partly fluid attenuated sequences, diffusion weighted imaging (DWI), susceptibility-weighted images (SWI) and Time of Flight (ToF) angiography are available. While ToF angiography visualizes microaneurysms and other arterial anomalies, SWI and DWI sequences detect vascular malformations, microbleeds, cavernomas, and/or active inflammatory or tumorous processes. For the spine program, a triplane T2 weighted sequence is available as an adjustment to possible findings as might be neural tube defects, lumbosacral variants or rheumatoid vertebral risk factors. If an applicant's screening is positively for any of these or other pathological findings relevant to aviation duties, he will be assessed unfit for flying and excluded from further consideration, unless there is a waiver option that may allow for an exception. Radiological details and imaging quality of the related cerebrospinal MRI sequences are displayed in **Table I**, and **Fig. 1**, respectively.

In this study, assimilable brain and spine sequences were applied for each period of time: in the pre-3-Tesla time period (2012 to 2015), the standard protocol lasted about 24 min, whereas in the period following introduction of the higher field strength technology (2016 to 2019), protocols required approximately 40 min of time. This was in part due to the inclusion of routine ToF angiography and SWI, which both were performed as optional sequences only before 2016.

Subjects

All examination results of German first-time applicants in the military aviation environment are routinely recorded in a two-tailed database, containing the complete flight-psychological and clinical-physiological (or pathological) test results. All applicants were free of any pre-existing clinical diagnoses or symptoms. Hence, all findings described in this study were detected by chance due to our screening procedure ("incidental findings"). For stratification in pre- and post-3-Tesla introduction periods, study subjects were allocated with regard to the years 2012 to 2015 (group 1), and 2016 to 2019 (group 2), respectively. No institutional review board (IRB) approval was required according to the regulations of the Bavarian chamber of physicians due to the anonymous and retrospective method of analysis. All study subjects had given written informed consent according to the Declaration of Helsinki in its actual revision. The consent included potential incidental findings in which case subjects were informed under psychological surveillance and referred to a clinical specialist, if necessary. Between 2012 and 2019, a total of 3315 screened study subjects were identified.

Data Acquisition

To explore diagnostically introduced changes over time using different imaging technologies, a database query was performed related to the terms of interest and covering the years from 2012 to 2019. Absolute and relative frequencies of case-related

Table I. Sequences of the German Air Force Imaging Screening Protocol used in 2012 and 2018.

SEQUENCES HEAD	1-TESLA (2012)	3-TESLA (2018)
T2-TSE	6 mm (tra) 3 mm (sag)	4 mm (cor) 2 mm (sag)
T1-TSE IR / T1-MPRAGE	2.5 mm (tra)	1 mm (tra) optional
T2-FLAIR	6 mm (cor)	4 mm (tra)
DWI	4 mm (tra) optional	4 mm (tra)
Hemo / SWI	6 mm (tra)	1.5 mm (tra)
ToF-Angio	1 mm (tra) + MIP optional	0.5 mm (tra) + MIP
SEQUENCES SPINE	**1-TESLA (2012)**	**3-TESLA (2018)**
T2-TSE	4 mm (sag) 4 mm (tra)	3 mm (sag) 3 mm (tra)
T2-STIR	5 mm (cor)	4 mm (cor)

incidental findings were recorded and chronologically displayed by years of occurrence. Incidental findings were restricted to cerebrospinal topographical locations and defined as previously undetected abnormalities of potential clinical relevance that were unexpectedly discovered and not necessarily related to the primary purpose of the examination.[22] The search strategy included a keyword query as well as ICD classification entries as recorded in the database on an anonymous basis.

Statistical Analysis

Statistical analysis was performed by an epidemiologist (FJ) using standard statistical software (Excel™, SPSS™, R®). For visualization of diagnostic frequencies, a semiquantitative approach was chosen, including transformation of numerical data into relative distributions. Following substratification of diagnostic entities as identified by the query, data were pooled according to their respective database entries before (before 2016) or after (2016 and later) introduction of the new 3-Tesla technology. Standard deviations and 95% confidence intervals were calculated for mean variance estimates of pooled data. Based on homoscedastic pooled standard deviations, an independent samples t-test was used for group comparison at alpha levels of 5% (significant) and 0.1% (highly significant). The effect size of group interdependencies was statistically approached by calculation of Cohen's d and Pearson's bivariate correlation coefficient (r).[6,32] All analyses were performed according to the principles of good epidemiological practice.[19]

RESULTS

From 2012 to 2019, a total of 3315 first-time applicants were assessed by MRI screening protocols as described before. Subjects eligible for assessment and further evaluation were, on average, 20.4 ± 3.8 (range, 15 to 45) years old, with more than 95% of them being male. Pre- and post-3-Tesla introductory groups did not differ significantly in age and proportions ($P < 0.001$; data shown in **Fig. 2**). Remarkably, as reported by other nations as well, there is an increasing number of applicants over 30 yr of age.[16,23]

The three diagnostic findings addressed in this study were intervertebral disc displacements (M51.2), malformations of cerebral vessels including nonruptured cerebral microaneurysms (Q28.3), and other abnormal findings of the central nervous system (CNS; R90.8), including white matter lesions, abnormal encephalogram, or arachnoid cysts. Where relative distributions were calculated, it could be shown that the majority of overall findings were located in the R90.8 group (**Fig. 3**), which may indicate a higher proportion of unusual and/or previously unseen incidental findings as compared to both of the remaining groups. In fact, pooled percentages for the observational period before vs. after introduction of the new technology statistically doubled in the R90.8 group (5.1% vs 9.8%), effective from 2016 and with its highest value in 2018 (13.5%; **Table II**).

Regression analysis revealed continuous rising percentages over time in all the diagnostic subgroups included in this study. According to the regression coefficient (R^2) as displayed in **Fig. 4**, the subgroup of "malformed cerebral vessels and cerebral microaneurysms" ($R^2 = 0.90$; $P = 0.0003$) exceeded the other subgroups with regard to other CNS abnormalities ($R^2 = 0.66$; $P = 0.014$) and intervertebral disc displacements ($R^2 = 0.81$; $P = 0.002$). From the statistical point of view, however, it has to be mentioned that the Q28.3 group with its highest R^2-coefficient is representing the group with the lowest prevalences at the same time, which may lead to misinterpretation due to low statistical power.

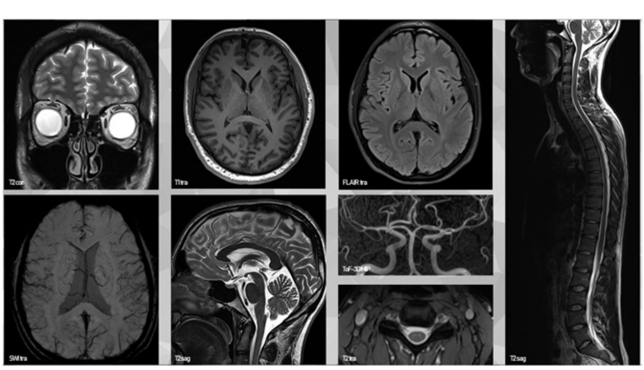


Fig. 1. MRI cerebrospinal sequences in the 3-Tesla protocol.

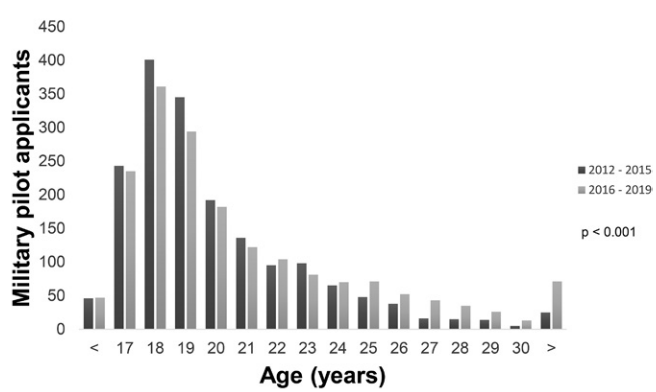


Fig. 2. Military pilot applicant distribution by age from 2012 to 2019.

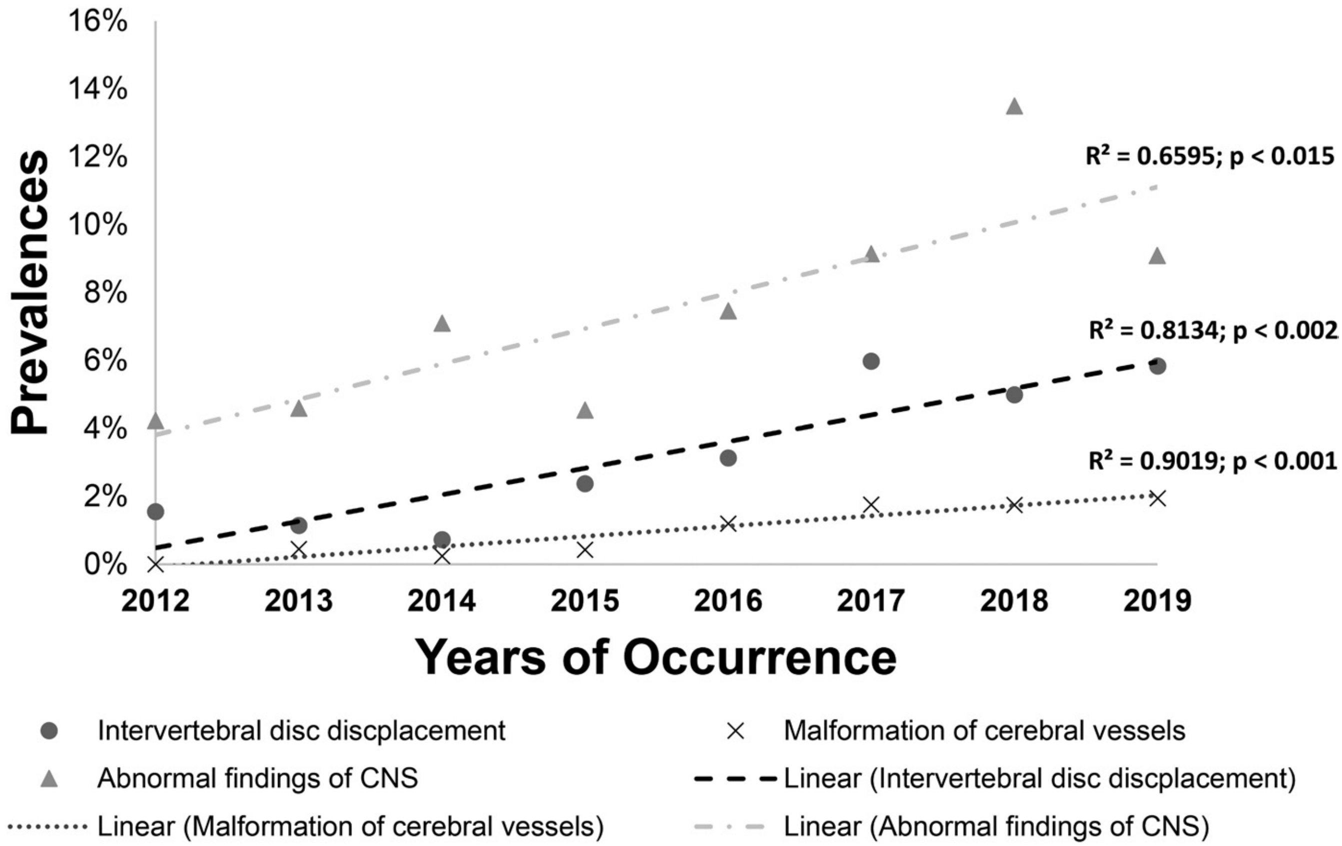


Fig. 3. Prevalence rates of incidental findings from 2012 to 2019 (R^2 = regression coefficient).

Conversion of pre- and post-3-Tesla observational periods into pooled groups (Fig. 4) demonstrated that the overall proportions of incidental findings essentially doubled when the new 3-T technology was introduced. Notably, this was true for all diagnostic groups which was confirmed by overall significant *t*-test results (Fig. 4). In spine MRI, for instance, incidences tripled with regard to intervertebral disc displacements [1.46 (CI: 1.17–1.74) % vs. 4.99 (4.69–5.29) %; $P = 0.00158$; df = 6]. In brain MRI, incidences of cerebral vessel malformations [0.28 (CI: 0.02–0.55) % vs. 1.67 (1.54–1.80) %; $P = 0.00018$; df = 6] as well as other abnormal CNS incidental findings [5.12 (CI: 4.84–5.40) % vs. 9.80 (9.39–10.22) %; $P = 0.00906$; df = 6] significantly increased by use of 3-Tesla MRI. Effect sizes and statistical correlations were strong in each condition analyzed (Cohen's d = $|-2.45|$; Pearson's r = $|-0.78|$).

DISCUSSION

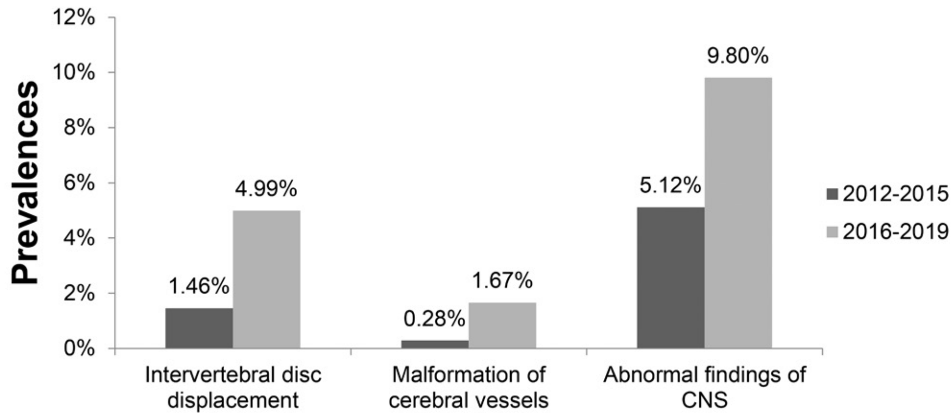
Our results indicate a significant increase of incidental cerebrospinal findings uncovered by implementation of a new and highly sensitive imaging technology in the assessment of military pilot applicants. The latter affects intervertebral disc displacement, malformation of cerebral vessels, and abnormal findings of the CNS.

Within the past 20 yr, MRI has become a clinical standard tool in brain and spine imaging. The lack of ionizing radiation

Table II. Unpooled Prevalences Of Relevant Neuroradiological Incidental Findings and Military Waiver.

YEAR	INTERVERTEBRAL DISC DISPLACEMENT M51.2 [*N*]	MALFORMATIONS OF CEREBRAL VESSELS Q28.3 [*N*]	OTHER ABNORMAL FINDINGS OF THE CNS R90.8 [*N*]	TOTAL [*N*]
2012	1.56% [7]	0.00% [0]	4.23% [19]	449
2013	1.15% [5]	0.46% [2]	4.60% [20]	435
2014	0.74% [3]	0.25% [1]	7.11% [29]	408
2015	2.38% [11]	0.43% [2]	4.55% [21]	462
2016	3.13% [13]	1.20% [5]	7.47% [31]	415
2017	5.99% [17]	1.76% [5]	9.15% [26]	284
2018	5.00% [20]	1.75% [7]	13.50% [54]	400
2019	5.84% [27]	1.95% [9]	9.09% [42]	462

ICD numbers relate to intervertebral disc displacements (M51.2), malformations of cerebral vessels (Q28.3), and other abnormal findings of the central nervous system (R90.8), respectively.



Outcome variables	t	df	SE	p
Intervertebral disc displacement	- 4.75	6	0.00745	0.0015
Malformation of cerebral vessels	- 7.19	6	0.00192	0.0001
Abnormal findings of CNS	- 3.22	6	0.01454	0.0091

Fig. 4. Pooled prevalence of three diagnostic entities as observed in 1- vs. 3-Tesla MRI screening. Statistical *t*-test results for two periods in three diagnostic entities. Calculated alpha levels: $P < 0.05$ significant; $P < 0.001$ highly significant (t = *t*-value, df = degrees of freedom, SE = pooled standard error, P = *P*-value).

makes MRI attractive for whole-body screening and has made a transition from 1-Tesla to 3-Tesla technology. The new technology includes advantages such as the field homogeneity and signal to noise ratio for a better resolution. However, as sensitivity improves rates of incidental findings rise.[17,31,34] Although rates as published are very dependent on outcome definitions, false-positive/-negative results and the population investigated, it is predictable that, in general, 3-Tesla MRI screening protocols will detect more incidental findings than 1- and 1.5-Tesla protocols.[5,30]

On the other hand, detection of unexpected incidental findings will always introduce medical and ethical concerns, particularly if the screened population consists of healthy volunteers.[10,21] In military and civilian pilot applicants, screening is primarily performed for flight safety, with the ultimate goal of preventing disease, sudden incapacitation, or loss of license. According to these prerequisites, it would be helpful to know the preconditions in detail that support or abort the preventive alignment of this process. However, there is still no common concept on how to handle subclinical radiological findings such as white matter lesions or asymptomatic intervertebral disc changes. In this study, we show that the rates of such incidental findings, using high-tech diagnostic scanners, might be considerably higher than previously thought.

Our study is based on a large sample of a highly homogeneous population of supposedly healthy German military volunteers, with more than 95% of them being male and about 80% between the ages of 17 to 23 yr. The MRI protocols have been developed and optimized over a 20-yr period in our institute and were uniformly applied to each pilot applicant. The reviewers were supervised by two senior radiologists with more than 25 yr of clinical experience; moreover, all findings were routinely discussed with in-house neurologic and orthopedic specialists and presented in daily grand rounds, making detection bias very unlikely. Consultation with relevant specialists is recommended.[35] Both scanners used were high-resolution, state-of-the-art 1- and 3-Tesla devices.

Our study has several limitations. First, due to the homogeneity of our study population, results may not be generalizable to populations of different age, gender, nationality, and socioeconomic state (sampling bias). This is a common problem when working with military recruits that is unavoidable.[9] Secondly, due to the internal focus on three entities (e.g., intervertebral disc dislocations, intracerebral vessel malformations, and other cerebral findings), a selection bias might have been introduced distorting statistical results. The final effect, however, must be considered minor since the vast majority of incidental findings is covered by our selection and the final conclusion is not affected through this bias. Thirdly, a center effect may have enhanced the prevalences of incidental findings reported in this study.[25] Additionally, any increasing subgroup trends could be due to some incremental improvements in the existing devices or increased reporting by the reading radiologists. Such tendencies of over-reporting are frequently seen in specialized institutions such as the German Air Force Centre of Aerospace Medicine, which is one of the largest centers of its kind in Europe. The only way to statistically control for this effect is to include calculation of relative outcome distributions within the population investigated and to compare with other centers specialized in the referring topics. It should be noted that whole-body MRI for military aviation screening is not widely available.[24] Fourthly, it is unlikely to suspect that flight candidates were sicker in 2019 than 2012.[7] Nevertheless, there is a diagnostic difference and increase for the in-house prevalences before 2002.[39,40]

In this study, we report a high number of 3-Tesla-related incidental cerebrospinal findings, the impact of which on flight performance, pilot healthiness, and military commitment is unclear. In case of intervertebral disc displacements, for instance, unexpected asymptomatic findings will not impair a pilot's health or performance as long as the anulus fibrosus is intact and radicular nerves are not affected. However, dependent on vibration, helmet weight, and other environmental risk factors, minor lesions may progress to disc herniation, protrusion and extrusion, causing major impairments such as neck and lower back pain in military pilots.[3,14] In this study, we found a pooled prevalence of asymptomatic disc displacements of 3.22% that is in line with most age-adjusted studies published so far.[2,36] In pre- vs. post 3-Tesla, however, more than double the number of incidental findings were seen in the pre-3-Tesla era [1.46% vs. 4.99%; $P < 0.05$). This raises the question of whether pilots with such findings will encounter serious problems during their flight careers, and if yes, what would be the percentage of clinical deterioration in later life. To our knowledge, no longitudinal studies so far have addressed this question.

With regard to intracerebral vessel malformation, the observation of increased diagnostic sensitivity is even more prominent: while in the pre-3-Tesla era, only neglectable amounts of incidental findings were diagnosed, occurrence rates detected with the 3-Tesla device increased to nearly the sixfold amounts ($0.28 \pm 0.2\%$ vs. $1.67 \pm 0.3\%$, $P < 0.001$). Although these numbers might have been selectively triggered by low statistical power within this group, the view on non-Q28.3 related intracerebral findings such as white matter lesions (WMH) confirms that this is in fact part of an iatrogenically generated problem introduced by increased technical device sensitivity. Similar to the results in spine MRI, brain imaging other than microvasculature-related MRI in this study revealed a considerable increase of incidental neuroradiological findings in the post-3-Tesla era as compared to earlier time periods (10.0 vs. 5.1%, $P < 0.05$). While most authors would agree that congenital microvascular malformations are not supposed to interfere with flight performance at any time, this point of view might change in case of a substantial finding; for example, white matter lesion of brain tissue, possibly representing a zone of microinfarction due to intrapartum asphyxia that has been present all the time, but cannot be seen by high-tech scanners inferior to the 3-Tesla.[12]

For individual applicants the unexpected diagnosis of an incidental finding, especially in the brain, may cause psychological stress, anxiety or confusion. Thus, in the Netherlands whole-body MRI screening is forbidden by law in civilian as well as in military persons.[35] However, in our opinion, the benefits for aviation safety outweigh these ethical concerns. In general, flight candidates must countersign informed consent about the possibility of potentially serious incidental findings and further diagnostic measures that might become necessary in such cases. In addition, candidates are informed about the potential occurrence of false-positive or false-negative findings although these percentages are exceedingly small in our experience.

From the aviation perspective, most aviation authorities agree that incidental findings have to be taken into account in any case. For civilian aviators, European Union Aviation Safety Agency (EASA) regulations require applicants for a class 1 medical certificate (professional aviation) to be assessed as unfit where a medical condition is likely to jeopardize the safe exercise of the privileges of the license.[8] Similarly, the Federal Aviation Administration (FAA) excludes any disease or condition that interferes with, or is aggravated by, flying or may reasonably be expected to do so.[13] In the case of military aviation, requirements are generally higher and restrictions closer; however, in all circumstances, the same principle rules: once a disease or medical condition is (newly) diagnosed, it has to be recorded by the medical assessor and forwarded to the licensing authority for further decision. This might support the epistemological hypothesis that in a no-disease screening for healthy pilots, no incidental findings will actually occur, unless diagnoses to be found (or excluded) are a priori prespecified. In aviation, individual demands are much higher than in most other occupations.

Hence, flight surgeons across the world have been trying to estimate the disease- or condition-inherent risk acceptable for flight safety concerns from a statistical point of view. The 1% rule as the known result of these efforts suggests that a 1% per annum risk of medical incapacitation be the threshold between acceptable and unacceptable preconditions.[29,37] To the aeromedical assessor, however, this will pose a major challenge considering the epidemiological skills required for this kind of calculation. As an alternative, we propose a classification system similar to the one that has been introduced by Langner et al. for nonaviation related populations.[26] In this system, findings are categorized in nonreportable norm variations (Cat. I), reportable findings requiring additional clarification (Cat. II), and actionable findings requiring urgent or emergency medical clarification (Cat. III). Furthermore, and independently from the general need of validation studies in the context of new technologies, an interdisciplinary consensus of critical or serious findings would be helpful for purposes of standardization and international harmonization.[15,20]

Our results show that the introduction of newer technology 3-Tesla MRI scanners providing high-resolution images to the GAF-ISP opened a gap toward incidental findings in pilots that cannot be closed due to missing aviation-related concepts. Incidental findings identified in this study were related to spine and brain neuroradiological imaging, including asymptomatic intervertebral disc dislocations and subclinical intracerebral changes such as vessel malformation and white matter lesions. Longitudinal studies on natural history and prognosis are needed, as well as clinical concepts on categorizing and risk estimate of such lesions in order to provide effective screening for future pilot selection.

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