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Deep vein thrombosis in response to stress induced by earthquakes in Japan: a meta-analysis of possible exacerbating factors

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The principal goal of this study was to assess factors associated with deep vein thrombosis (DVT) in the aftermath of earthquakes in Japan. We searched PubMed, Google Scholar, Web of Science, and Cochrane Library for articles published in English or Japanese regarding indicators for DVT associated with Japanese earthquakes. We calculated pooled odds ratios (OR) or mean differences (MD) with 95% confidence intervals (CIs) for patients with DVT (the DVT group) as compared with the non-DVT group for potential predictors. Ultimately, 7 articles were included in the analysis, comprising 6,637 subjects (DVT, 895; and non-DVT, 5,742). The following factors proved statistically significant: female gender (OR = 1.48, 95% CI; 1.20–1.81, $p = 0.0002$), greater age (MD = 4.44, 95% CI; 1.62–7.25, $p = 0.002$), hypertension (OR = 1.44, 95% CI; 1.18–1.75, $p = 0.0003$), heart disease (OR = 1.45, 95% CI; 1.07–1.97, $p = 0.02$), previous history of DVT (OR = 9.23, 95% CI; 2.94–28.91, $p = 0.0001$), sleeping pill use (OR = 1.81, 95% CI; 1.37–2.38, $p = 0.0001$), lower leg varix (OR = 1.63, 95% CI; 1.17–2.28, $p = 0.004$), and soleal vein dilatation ≥ 8 mm (OR = 2.13, 95% CI; 1.32–3.42, $p = 0.002$). Our findings furnish insights that can aid in making informed choices about healthcare and policy in the context of earthquake-induced stress.

Keywords Deep vein thrombosis, Pulmonary thromboembolism, Japan, Meta-analysis, Earthquake

Deep vein thrombosis (DVT) has attracted global public attention as a disease exacerbated by disasters[1–14]. Importantly, an elevated risk of DVT has been reported among earthquake evacuees: 9.1–27.1% among earthquake evacuees globally, 10.3–27.1% among Japanese evacuees, and 6.0–20.0% among non-Japanese[1–7,14], 0.8–22.3% among patients with trauma (1.8% in patients with burns and 0.8–22.3% in patients with hip fractures)[15–17], and 1.3–9.3% among the general population from a Danish national cohort (1.9–9.3% in women and 1.3–8.1% in men)[18]. The incidence of DVT often rises after earthquakes due to a combination of immobility, stress, dehydration, and disrupted healthcare access[1–7]. Survivors frequently endure prolonged immobility in shelters or cars, which increases blood stasis and the risk of clot formation. Stress and trauma from the disaster can alter blood coagulation, while dehydration thickens the blood, further elevating the risk of DVT. Older adults and those with pre-existing health conditions are particularly vulnerable. The lack of timely medical care in the aftermath exacerbates these risks, underscoring the need for targeted disaster preparedness and response measures. Among DVT cases, 33.5% occur concomitantly with pulmonary thromboembolism[19,20], and as many as 9.7% of these result in sudden death within a month[21]. In other words, DVT can have serious consequences shortly after earthquakes. Therefore, early detection and prevention of DVT are imperative, especially among earthquake evacuees.

When assessing predictors of DVT in earthquake scenarios, it is imperative to approach Japanese and other populations separately due to considerations related to geography, demographic composition, and genetic factors. There are three primary reasons for this distinction. First, Japan is a seismic hotspot, frequently experiencing earthquakes, like the 2011 Great East Japan earthquake and the 2016 Kumamoto earthquake[22–24]. Forecasts

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predict that the Tokyo metropolitan area is at risk of a significant earthquake in the near future, prompting formulation of countermeasures[22]. Second, since 2005, Japan has had the world's most aged population. This trend is projected to intensify in the future. Estimates project that the percentage of individuals aged 65 and over will surge to 30.8% by 2030, 34.8% by 2040, and eventually reaching 37.1% by 2050[25,26]. Third, genetic factors linked to DVT differ between Japanese and other ethnic groups[27]. Japanese have a relatively lower risk of DVT than African Americans because of genetics[28], including PROS1[29–33], PROC[29–33], SERPINC1[29–33], prothrombin G20210A[34–36], and a protein S mutation, K196E[37,38]. Furthermore, Japanese are reported to have a relatively lower risk of DVT compared to Caucasians[28], primarily due to genetic differences such as Factor V Leiden[34–36], a mutation that increases DVT risk and is more common in Caucasians.

Several investigations have explored markers for DVT in the aftermath of Japanese earthquakes[1–13]. Nevertheless, a consensus on this urgent matter has not yet been achieved. Therefore, the goal of this study was to assess factors associated with DVT in the aftermath of Japanese earthquakes.

Methods

Search strategy

The meta-analysis protocol for this study has been registered with the International Prospective Register of Systematic Reviews (PROSPERO registration no. CRD42023458641). The meta-analysis was conducted in accordance with guidelines of the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA)[39].

Our search examined PubMed, Google Scholar, Web of Science, and the Cochrane Library to identify pertinent, peer-reviewed original articles published in either English or Japanese, focusing on factors associated with DVT in the context of a Japanese earthquake. Searches were performed on August 30, 2023. Search terms included: (deep vein thrombosis [Title/Abstract]) AND (earthquake [Title/Abstract]). All journals published as of August 30, 2023 were included in the search. In addition, we explored unpublished or gray literature as part of our meta-analysis. We further screened the reference lists of studies identified via the database search. During the curation process, we excluded articles that did not perform comparative analyses of forecasting indicators between individuals with and without DVT following a Japanese earthquake (i.e., lack of evaluable data), articles categorized as review articles, case reports ($n < 9$), commentaries, editorials, insights articles, and proceedings. To ensure rigor, two researchers (YF and TK) independently executed database searches, reviewed articles, and resolved any differences through discussions.

Data extraction

Data extraction encompassed retrieval of the following variables: primary author, year of publication, study design, seismic event, characteristics of subjects (comprising sample size, age distribution, and gender distribution), DVT diagnosis, DVT incidence rate, and factors associated with DVT. We focused on retrieval of factors shared by two or more articles, with specific attention given to variables such as female gender (categorical variable), age (numerical variable, years), smoking (categorical variable), drinking (categorical variable), exercise habits (categorical variable), hypertension (categorical variable), diabetes (categorical variable), dyslipidemia (categorical variable), heart disease (categorical variable), cancer (categorical variable), insomnia (categorical variable), previous history of DVT (categorical variable), hospitalization or surgery < 3 months (categorical variable), sleeping pill use (categorical variable), anti-coagulant or platelet agent (categorical variable), trauma (categorical variable), systolic blood pressure (numerical variable, mmHg), diastolic blood pressure (numerical variable, mmHg), lower leg varix (categorical variable), lower leg edema (categorical variable), lower leg pain (categorical variable), lower leg skin flare (categorical variable), overnight stay in a car (categorical variable), temporary housing resident (categorical variable), walking time shortened (categorical variable), reduced urination (categorical variable), and soleal vein dilatation ≥ 8 mm (categorical variable). Two researchers (YF and TK) conducted data extraction independently and resolved any differences through discussion.

Risk of bias assessment

As studies eligible for inclusion lacked randomization, we conducted a quality assessment using the Newcastle-Ottawa Scale, adapted for cross-sectional studies[40,41]. Assessment considered the following issues: (1) selection, which evaluated the representativeness of the sample, sample size, treatment of non-respondents, and accuracy of exposure ascertainment; (2) comparability, which assessed the degree to which confounding factors were controlled in the analysis; and (3) outcome, encompassing both evaluation of the outcome itself and appropriate use of statistical tests. The maximum possible score was 10 points: 5 points for selection, 2 points for comparability, and 3 points for outcome assessment. These cumulative scores categorized studies as: 0–4 (unsatisfactory), 5–6 (satisfactory), 7–8 (good), and 9–10 (high), respectively. Throughout this evaluation process, YF and TK independently assessed the studies using the Newcastle-Ottawa Scale and any disparities were resolved through discussions.

Risk of reporting bias assessment

The potential for reporting bias was also evaluated based on whether included studies had financial conflicts of interest. Furthermore, we visually assessed the risk of reporting bias using a funnel plot, with gender as a representative variable. YF and TK independently appraised bias and any disparities were resolved through discussions.

Grading the quality of evidence

The Grading of Recommendations Assessment, Development, and Evaluation (GRADE) method was used to assess the quality of evidence for each outcome of the meta-analysis[42–48]. Levels of quality of evidence recommended by the GRADE Working Group were defined as high, moderate, low, and very low. Judgments were based on the risk of bias, inconsistency, indirectness, imprecision, and publication bias.

Statistical analyses

For the meta-analysis, we employed Review Manager Software version 5.3 (The Cochrane Collaboration, Oxford, United Kingdom).

Pooled prevalence was calculated using the inverse variance method, as previously reported[49]. A random effects model was used for meta-analysis due to high heterogeneity between studies ($I^2 > 95\%$, $p < 0.05$) and depicted using a forest plot. Prior to meta-analysis, the standard error (SE) for each prevalence estimate was calculated using the formula $SE = \sqrt{p(1-p)/n}$ where p = the proportion of individuals diagnosed with DVT and n = total sample size for the study.

Categorical variables were entered with counts of events and counts of subjects, whereas numerical variables were entered with mean values and standard deviations and counts of subjects. To gauge heterogeneity levels, we utilized both the X^2 test and I^2 statistics, categorizing them as insignificant (I^2 0% to < 25%), low (I^2 25% to < 50%), or significant (I^2 50–100%). In instances where significant heterogeneity was observed ($I^2 > 50\%$ and $p < 0.10$), we used a random-effects model for the analysis. Otherwise, the fixed-effects model was applied. Odds ratios (ORs) with 95% confidence intervals (CIs) were used to evaluate binary variables, and mean differences (MDs) with 95% CIs were used for continuous variables. A p-value of < 0.05 was considered significant. Statistical analyses were conducted by one researcher (TK).

Sensitivity analysis

Following evaluation using the Newcastle-Ottawa Scale, a sensitivity analysis was performed exclusively on good or very good quality studies.

Results

Search results

A graphical representation of this selection process is provided in Fig. 1. In total, 18 articles were identified via PubMed, 9 articles were procured from Google Scholar, 12 were obtained from Web of Science, and 2 were acquired from the Cochrane Library. Among these, 7 duplicates were excluded. After initial screening by title and abstract, 34 articles were considered, leading to exclusion of 21 articles that were deemed irrelevant. Subsequently, 13 full text articles were evaluated, resulting in exclusion of another 6 articles due to lack of evaluable data[8–13]. Ultimately, 7 articles were included in the analysis, encompassing 6,637 subjects, 895 with DVT and 5,742 without (Table 1).

All of the included articles reported cross-sectional studies. Onishi et al.[1] assessed 207 evacuees in shelters (female, 159 individuals; mean age, 68.1 years) living in Kumamoto Prefecture after the 2016 Kumamoto earthquake (April 27 2016 and May 3–4 2016) and found a DVT prevalence of 11.1% (23/207 individuals). Onishi et al.[2] assessed 290 evacuees (female, 226 individuals; mean age, 71.9 years) living in Miyagi Prefecture 44 months after the 2011 Great East Japan earthquake and reported a DVT prevalence of 10.3% (30/290 individuals). Onishi et al.[3] investigated 181 evacuees (female, 141 individuals; mean age, 73.9 years) living in Kumamoto Prefecture over a period of 19 months after the 2016 Kumamoto earthquake (May 3–4 2016, December 24–25 2016, and November 3–4 2017), finding a DVT prevalence of 14.9% (27/181 individuals). Ueda et al.[4] assessed 701 hospitalized patients (female, 474 individuals; mean age, 67.7 years) one month after the Great East Japan earthquake and found a DVT prevalence of 27.1% (190/701 individuals). Sato et al.[5] also assessed 1673 evacuees (female, 1225 individuals; mean age, 70.4 years) one month after the Kumamoto earthquake and reported a DVT prevalence of 10.6% (178/1673 individuals). Shibata et al.[6] assessed 269 evacuees living in Miyagi Prefecture (female, 174 individuals; 70.6 years) one month after the 2011 Great East Japan earthquake and found a DVT incidence of 24.2% (65/269 individuals). Shibata et al.[7] assessed 3316 evacuees living in Iwate Prefecture (female, 2633 individuals; 71.0 years) one month after the 2011 Great East Japan earthquake and found a DVT incidence of 11.5% (382/3316 individuals).

Risk of bias

In Table 2, Newcastle-Ottawa Scale scores for selected cross-sectional studies are presented. Scores varied between 5 and 8 (Supplementary Table S1–S7); thus, the quality of the meta-analysis was acceptable.

Risk of reporting bias

Two articles[2,7] reported financial conflicts of interest, suggesting a potential for reporting bias. However, the funnel plot for the female gender variable (Fig. 2) displayed values within the acceptable range and positioned close to the no-effect line. Accordingly, the degree of reporting bias was considered acceptable.

Grading the quality of evidence

Table 3 shows the GRADE evidence profiles. The GRADE level of evidence is high for cancer and hospitalization or surgery < 3 months; moderate for female gender, anti-coagulant or platelet agent, systolic blood pressure, and diastolic blood pressure; low for age, smoking habit, drinking habit, heart disease, previous history of DVT, sleeping pill use, and lower leg varix; and very low for exercise habits, hypertension, diabetes, dyslipidemia, insomnia, trauma, lower leg edema, lower leg pain, lower leg skin flare, overnight stay in a car, temporary housing resident, walking time shortened, reduced urination, and soleal vein dilatation ≥ 8 mm.

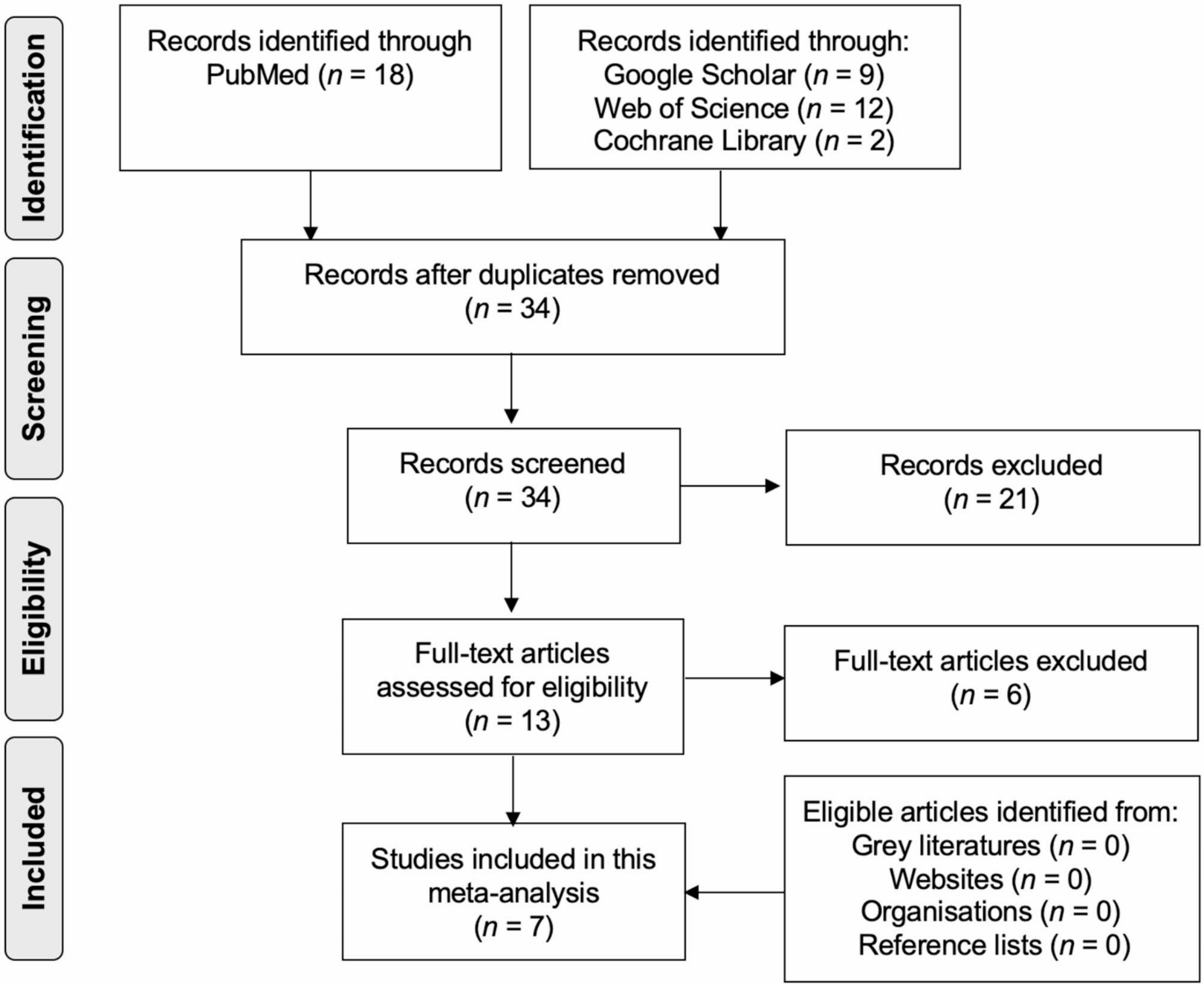

Fig. 1. PRISMA flowchart describing article selection. *PRISMA*, preferred reporting items for systematic reviews and meta-analyses.

		Subject			Earthquake		DVT		
Study	Study design	Number (male/female)	Mean age (years)	Setting	Name	Post-earthquake period (months)	Site	Diagnosis	Incidence
Onishi et al., 2017[1]	Cross-sectional	207 (48/159)	68.1	Evacuees in shelters	2016 Kumamoto	NA	Calf	US	11.1% (23/207)
Onishi et al., 2020[2]	Cross-sectional	290 (64/226)	71.9	Evacuees in temporary housings	2011 Great East Japan	44	Calf	US	10.3% (30/290)
Onishi et al., 2022[3]	Cross-sectional	181 (40/141)	73.9	Evacuees in shelters and temporary housings	2016 Kumamoto	3–19	Calf	US	14.9% (27/181)
Ueda et al., 2014[4]	Cross-sectional	701 (227/474)	67.7	Hospitalized patients with PTE	2011 Great East Japan	1	Calf	US	27.1% (190/701)
Sato et al., 2019 [5]	Cross-sectional	1673 (448/1225)	70.4	Evacuees in shelters	2016 Kumamoto	1	Calf	US	10.6% (178/1673)
Shibata et al., 2014[6]	Cross-sectional	269 (95/174)	70.6	Evacuees in shelters	2011 Great East Japan	1	Calf	US	24.2% (65/269)
Shibata et al., 2017[7]	Cross-sectional	3316 (683/2633)	71.0	Evacuees in shelters	2011 Great East Japan	1	Calf	US	11.5% (382/3316)

Table 1. Characteristics of selected studies. *DVT*, deep vein thrombosis; *PTE*, pulmonary thromboembolism; *NA*, not available; *US*, ultrasonography.

Study	Selection	Comparability	Outcome	Total score
Onishi et al., 2017[1]	★★★	★★	★★★	8 (Good)
Onishi et al., 2020[1]	★★★	★★	★★★	8 (Good)
Onishi et al., 2022[1]	★★	★★	★★★	7 (Good)
Ueda et al., 2014[1]	★★★		★★	5 (Satisfactory)
Sato et al., 2019[1]	★★★★	★★	★★★	9 (Very good)
Shibata et al., 2014[1]	★★★		★★★	6 (Satisfactory)
Shibata et al., 2017[1]	★★★		★★★	6 (Satisfactory)

Table 2. Quality assessment of the eligible studies based on the Newcastle–Ottawa Scale for cross-sectional studies.

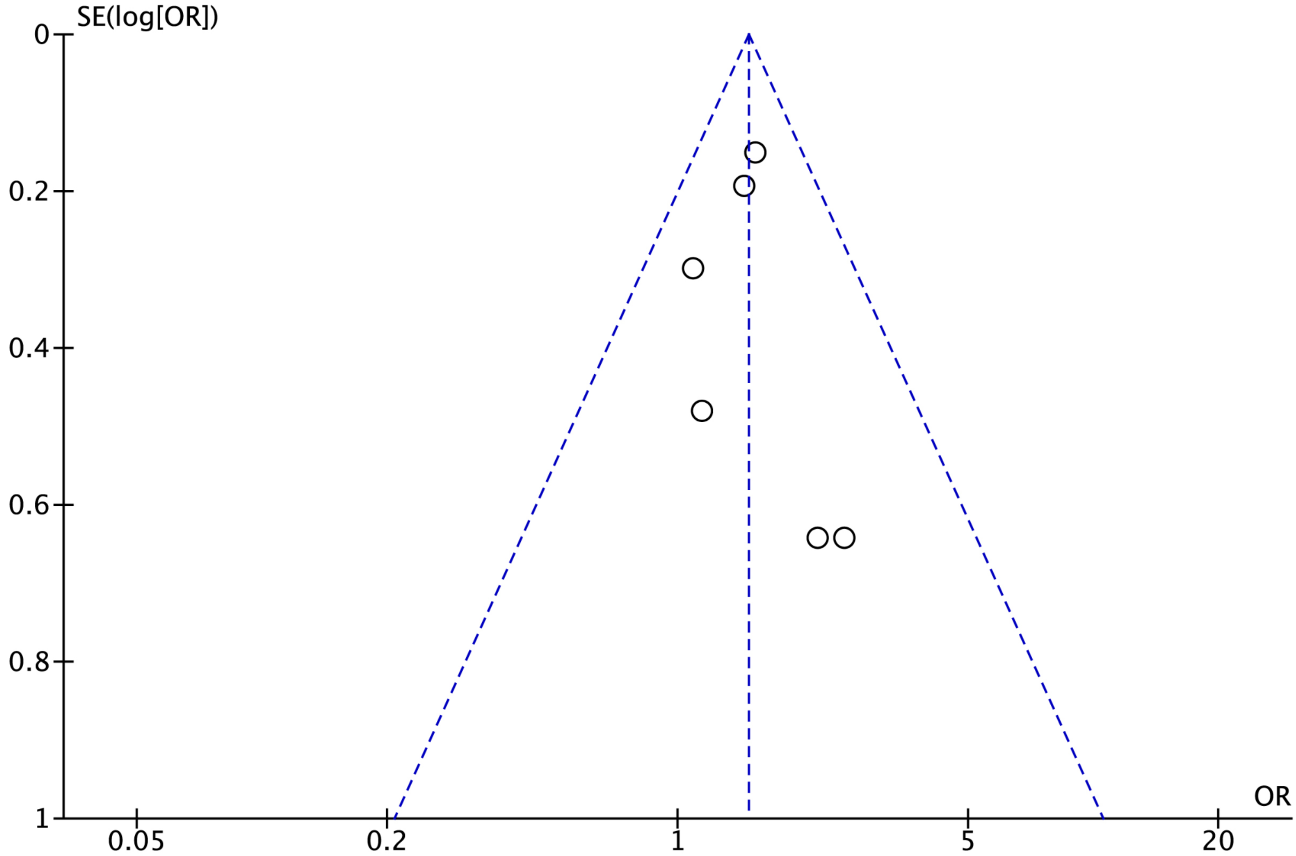

Fig. 2. All data points for female gender fall within predefined limits.

Meta-analysis results

Results of the meta-analysis (Fig. 3) showed an overall pooled prevalence of DVT of 15.67 (95% CI, 11.68 to 19.66).

Significant heterogeneity was observed in age ($I^2=88\%$, $p<0.00001$), exercise habits ($I^2=62\%$, $p=0.05$), insomnia ($I^2=83\%$, $p=0.02$), trauma ($I^2=80\%$, $p=0.07$), lower leg edema ($I^2=80\%$, $p<0.07$), temporary housing resident ($I^2=96\%$, $p<0.00001$), and reduced urination ($I^2=81\%$, $p=0.001$). Consequently, a random-effects model was employed to analyze these factors. However, for other factors, no significant heterogeneity was observed, and a fixed-effects model was utilized.

Statistical significance was observed for the following factors: female gender (pooled OR = 1.48, 95% CI; 1.20–1.81, $p=0.0002$), older age (pooled MD = 4.44, 95% CI; 1.62–7.25, $p=0.002$), presence of hypertension (pooled OR = 1.44, 95% CI; 1.18–1.75, $p=0.0003$), heart disease (pooled OR = 1.45, 95% CI; 1.07–1.97, $p=0.02$), previous history of DVT (pooled OR = 9.23, 95% CI; 2.94–28.91, $p=0.0001$), sleeping pill use (pooled OR = 1.81, 95% CI; 1.37–2.38, $p=0.0001$), lower leg varix (pooled OR = 1.63, 95% CI; 1.17–2.28, $p=0.004$), and soleal vein dilatation ≥ 8 mm (pooled OR = 2.13, 95% CI; 1.32–3.42, $p=0.002$). However, no statistical significance was observed in other factors (Figs. 4, 5, 6, 7 and 8).

Outcome	Quality
Female gender	Moderate (⊕⊕⊕◯)
Age	Low (⊕⊕◯◯)
Smoking habit	Low (⊕⊕◯◯)
Drinking habit	Low (⊕⊕◯◯)
Exercise habits	Very low (⊕◯◯◯)
Hypertension	Very low (⊕◯◯◯)
Diabetes	Very low (⊕◯◯◯)
Dyslipidemia	Very low (⊕◯◯◯)
Heart disease	Low (⊕⊕◯◯)
Cancer	High (⊕⊕⊕⊕)
Insomnia	Very low (⊕◯◯◯)
Previous history of DVT	Low (⊕⊕◯◯)
Hospitalization or surgery <3 months	High (⊕⊕⊕⊕)
Sleeping pill use	Low (⊕⊕◯◯)
Anti-coagulant or platelet agent	Moderate (⊕⊕⊕◯)
Trauma	Very low (⊕◯◯◯)
Systolic blood pressure	Moderate (⊕⊕⊕◯)
Diastolic blood pressure	Moderate (⊕⊕⊕◯)
Lower leg varix	Low (⊕⊕◯◯)
Lower leg edema	Very low (⊕◯◯◯)
Lower leg pain	Very low (⊕◯◯◯)
Lower leg skin flare	Very low (⊕◯◯◯)
Overnight stay in a car	Very low (⊕◯◯◯)
Temporary housing resident	Very low (⊕◯◯◯)
Walking time shortened	Very low (⊕◯◯◯)
Reduced urination	Very low (⊕◯◯◯)
Soleal vein dilatation ≥8 mm	Very low (⊕◯◯◯)

Table 3. GRADE evidence profile.

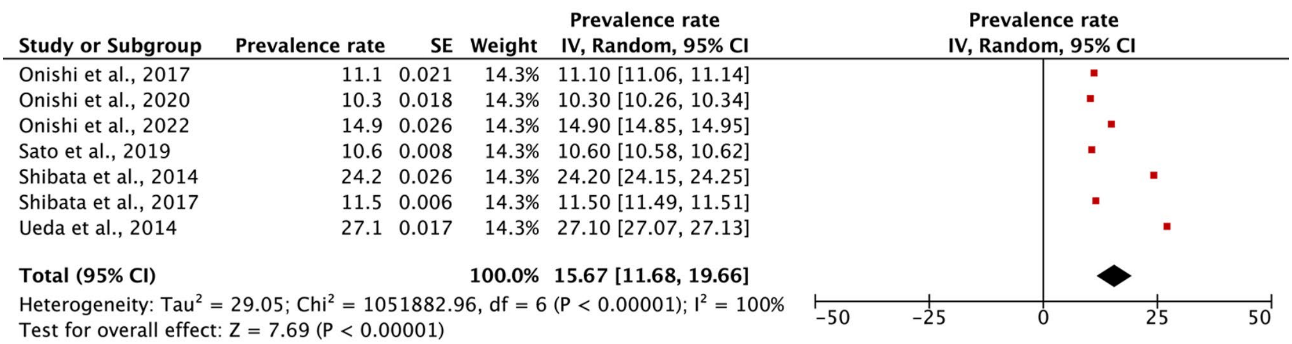

Fig. 3. Pooled prevalence of DVT was 15.67 (95% CI, 11.68 to 19.66). *DVT*, deep vein thrombosis; *SE*, standard error; *CI*, confidence interval.

Sensitivity analysis

Following an evaluation using the Newcastle-Ottawa Scale, a sensitivity analysis was performed, focusing on good[1–3] and very good studies[5]. To be more precise, 4 articles[1–3,5] were included in the sensitivity analysis, comprising 2,351 subjects, of whom 258 had DVT and 2,093 did not. Results of the sensitivity analysis were similar to those from the main analysis, except for dyslipidemia (Table 4). This sensitivity analysis confirms the robustness of our findings.

Discussion

We first synthesized evidence concerning factors associated with DVT in the context of Japanese earthquakes. Notably, significant factors associated with DVT included female gender, advanced age, hypertension, heart disease, prior history of DVT, use of sleeping pills, lower leg varix, and soleal vein dilatation ≥ 8 mm. No statistically significant associations were observed for the remaining factors.

In our meta-analysis, the overall pooled prevalence of DVT was 15.67 (95% CI, 11.68 to 19.66). Sahebi et al.[14] reported that the overall pooled prevalence of DVT was 11.43 (95% CI, 9.06 to 13.79) in Japanese general population and 2.51 (95% CI, 0.40 to 4.63) in patient survivors living in Pakistan, China, or Nepal. Reasons for differences in DVT prevalence among Asian countries require further investigation.

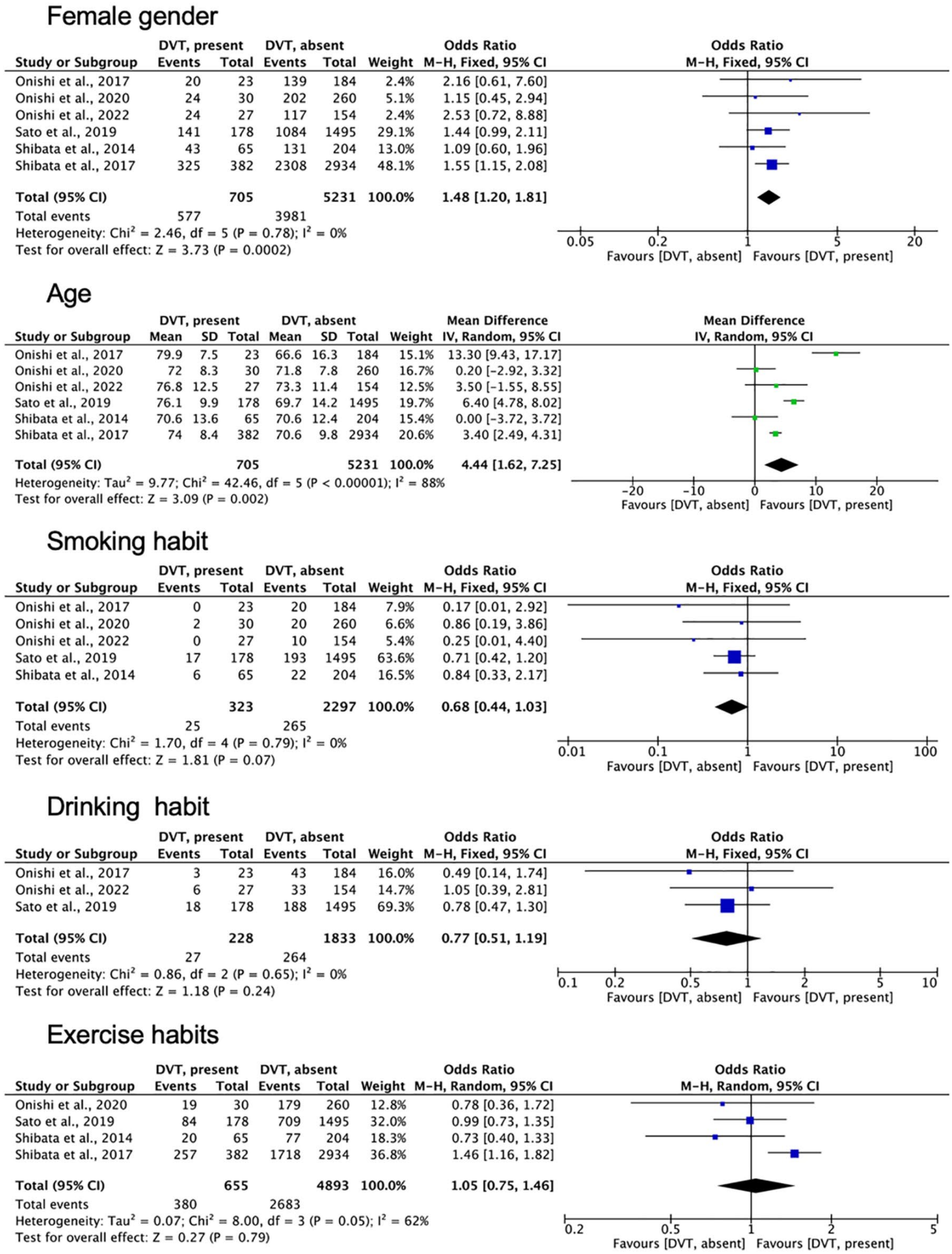

Fig. 4. Female gender and advanced age demonstrated significant associations with DVT following Japanese earthquakes (female gender [pooled OR = 1.48, p = 0.0002], older age [pooled MD = 4.44, p = 0.002]). *DVT*, deep vein thrombosis; *OR*, odds ratio; *MD*, mean difference.

Female gender and advanced age were significant factors associated with DVT. Comparable outcomes were noted in prior studies involving trauma patients[17]. The mechanism remains unclear[1–3,5–7], although potential explanations encompass reduced activity due to aging and pregnancy. This information could help to explain the incidence of DVT following earthquakes in Japan.

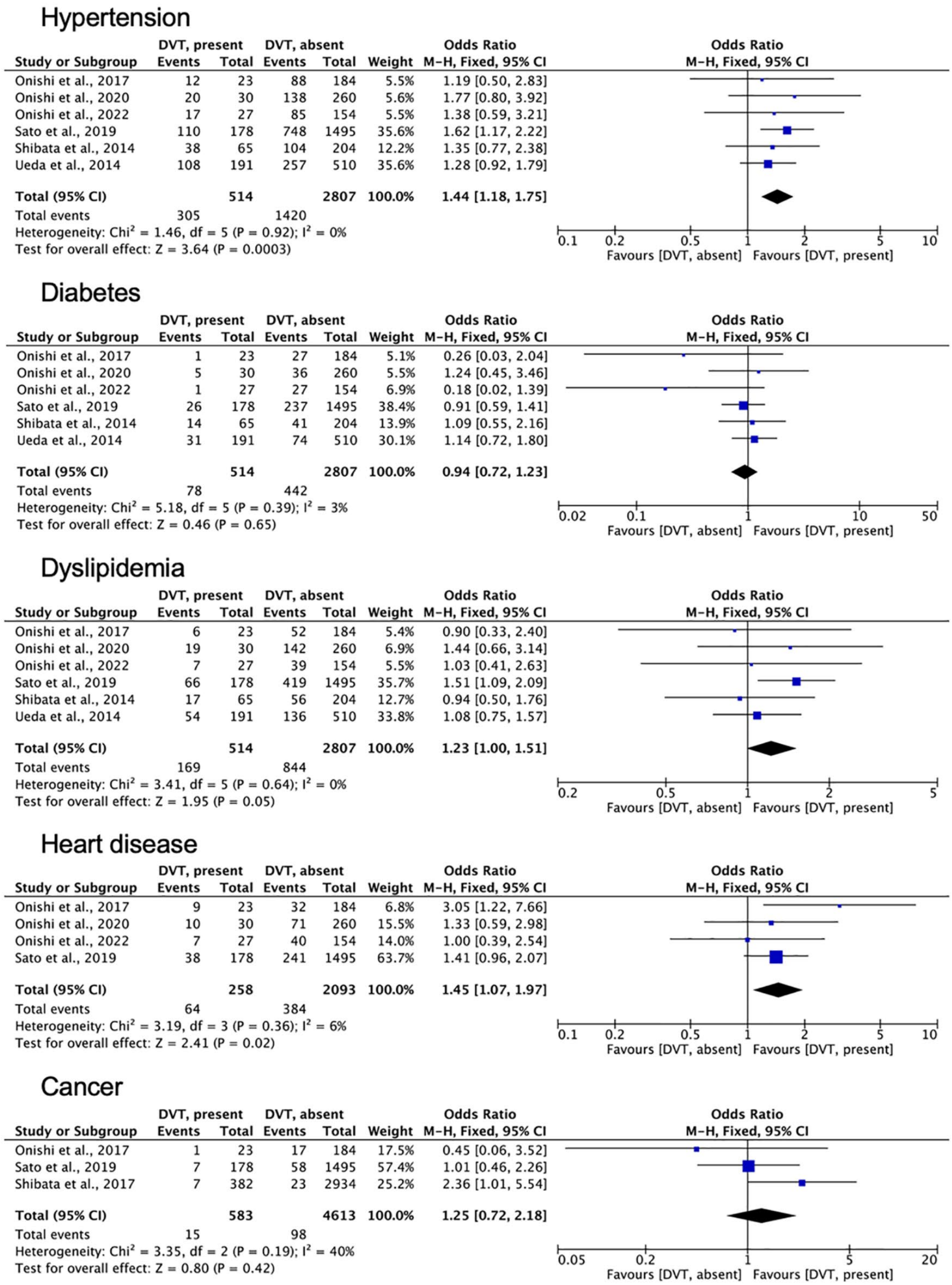

Fig. 5. Hypertension, dyslipidemia, and heart disease demonstrated significant associations with DVT following Japanese earthquakes (presence of hypertension [pooled OR = 1.44, $p = 0.0003$], dyslipidemia [pooled OR = 1.23, $p = 0.05$], heart disease [pooled OR = 1.45, $p = 0.02$]). *DVT*, deep vein thrombosis; *OR*, odds ratio.

Interestingly, hypertension was significantly associated with DVT, in contrast to systolic and diastolic blood pressure. The distinction between short-term hypertension (including white-coat hypertension) and long-term hypertension could be important[50]. In rats, hypertension lasting over 3 weeks increased the counts of granulocytes, monocytes, macrophages, and lymphocytes. It also elevated MMP-2 and MMP-9 levels within the pressurized

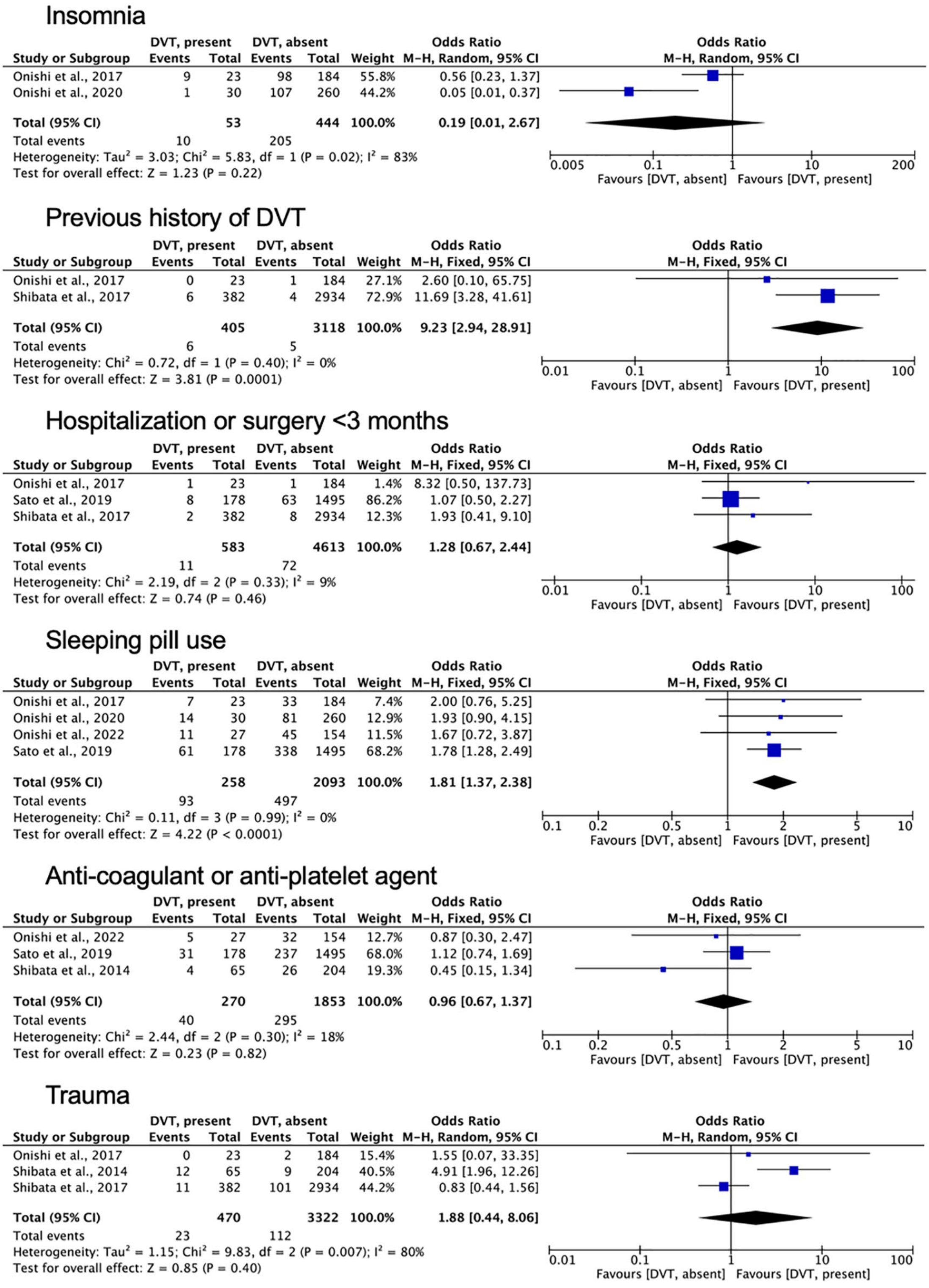

Fig. 6. Previous history of DVT and sleeping pill use demonstrated significant associations with DVT following Japanese earthquakes (previous history of DVT [pooled OR = 9.23, $p = 0.0001$], sleeping pill use [pooled OR = 1.81, $p = 0.0001$]). *DVT*, deep vein thrombosis; *OR*, odds ratio.

venous valve, inducing valve remodeling (loss and regurgitation)[51–55], and contributed to the incidence of DVT. Hence, a prolonged history of hypertension rather than acute hypertension after an earthquake, increases the likelihood of DVT immediately after an earthquake.

Heart disease, lower leg varix, and soleal vein dilatation ≥ 8 mm were associated with DVT. While a specific causal relationship between heart disease and DVT remains uncertain due to inconsistencies in provided

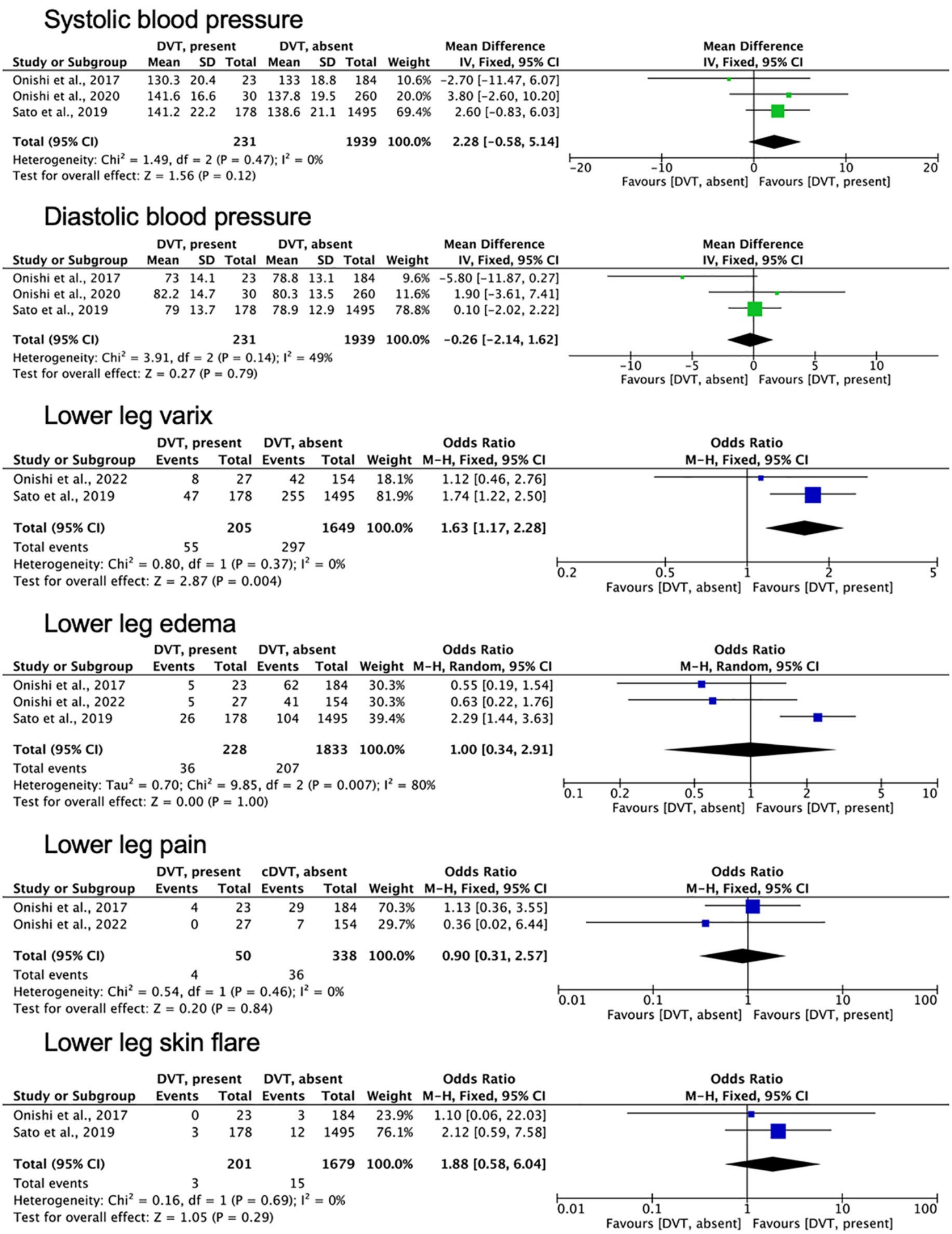

Fig. 7. Lower leg varix demonstrated a significant association with DVT following Japanese earthquakes (lower leg varix [pooled OR = 1.63, $p = 0.004$]). *DVT*, deep vein thrombosis; *OR*, odds ratio.

definitions in the literature, it has been reported that reduced venous return resulting from heart disease can lead to blood flow stasis, potentially contributing to development of soleal vein varix[56,57]. Moreover, previous studies have demonstrated a noteworthy connection between varicose veins and DVT[57]. One possible explanation is that individuals with varicose veins often exhibit elevated levels of inflammatory and prothrombotic markers, potentially contributing to DVT[57]. The soleal vein, located deep in the calf muscle, is particularly susceptible to thrombosis due to its anatomy, increasing the likelihood of blood stasis and clot formation[58]. Soleal vein dilation

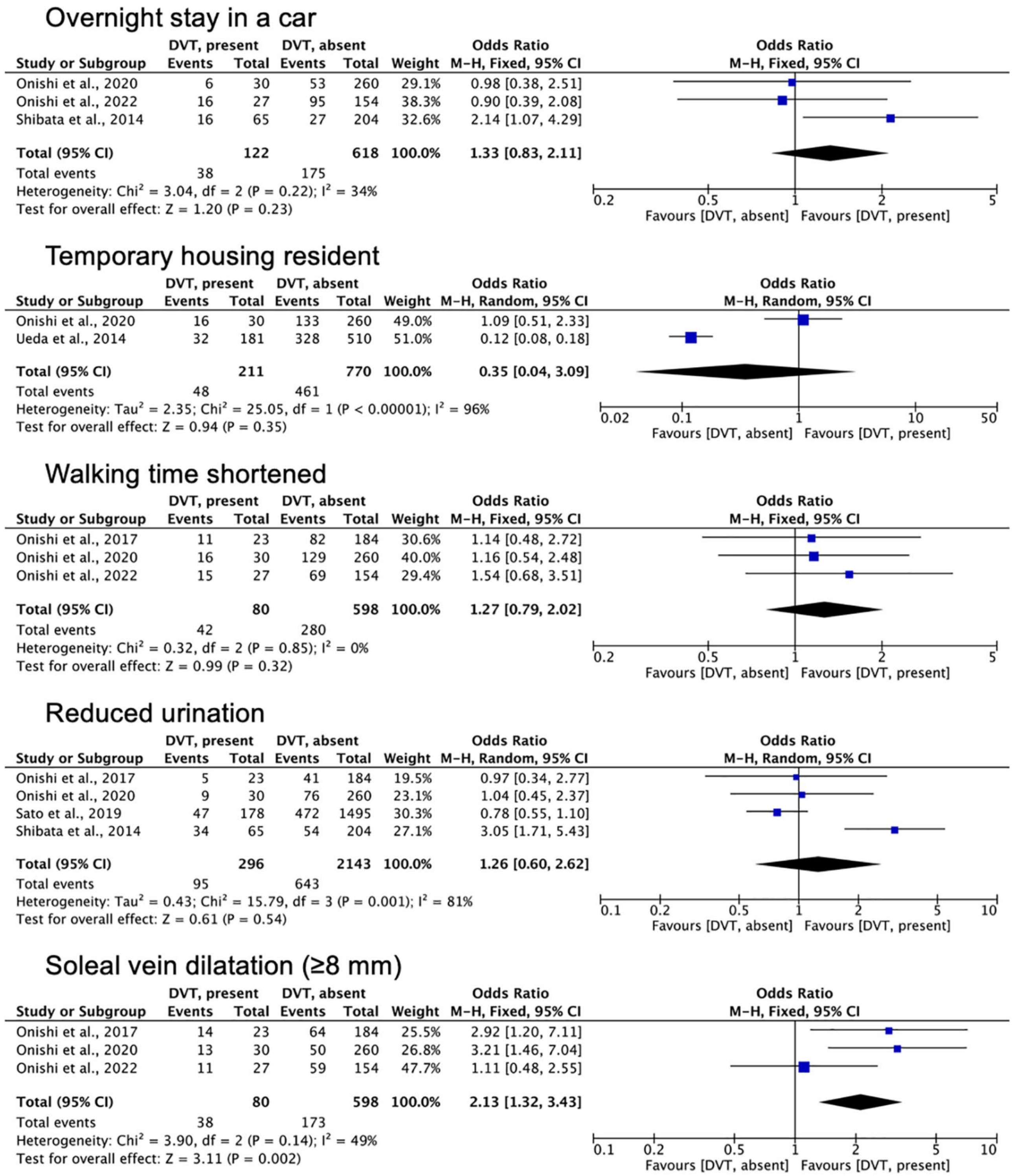

Fig. 8. Soleal vein dilatation (≥ 8 mm) demonstrated a significant association with DVT following Japanese earthquakes (soleal vein dilatation ≥ 8 mm [pooled OR = 2.13, $p = 0.002$]). *DVT*, deep vein thrombosis; *OR*, odds ratio.

is associated with severe outcomes such as proximal DVT, pulmonary embolism, and recurrent DVT[59]. However, in our meta-analysis, all included studies were conducted with a cross-sectional design; thus, the longitudinal relationship between DVT and these medical conditions remains unclear. In theory, it is particularly important to be concerned about DVT if both these medical conditions are present, as cross-sectional relationships are significant in our meta-analysis.

	Studies	Subjects	Statistical heterogeneity		Effects model	Pooled OR or MD	95% CI	*p* value
			I^2 (%)	*p* value				
Female gender	4	2,351	89	< 0.00001	Random	5.85	1.05 to 10.65	0.02
Age	4	2,351	0	0.72	Fixed	1.52	1.09 to 2.10	0.01
Smoking habit	4	2,351	0	0.67	Fixed	0.64	0.40 to 1.03	0.07
Drinking habit	3	2,061	0	0.65	Fixed	0.77	0.51 to 1.19	0.24
Exercise habits	2	1,963	0	0.58	Fixed	0.96	0.72 to 1.28	0.78
Hypertension	4	2,351	0	0.90	Fixed	1.56	1.20 to 2.04	0.001
Diabetes	4	2,351	29	0.24	Fixed	0.79	0.54 to 1.80	0.23
Dyslipidemia	4	2,351	0	0.70	Fixed	1.39	1.06 to 1.83	0.02
Heart disease	4	2,351	6	0.36	Fixed	1.45	1.07 to 1.97	0.02
Cancer	2	1,880	0	0.46	Fixed	0.88	0.42 to 1.86	0.74
Insomnia	2	497	83	0.02	Random	0.19	0.01 to 2.67	0.22
Hospitalization or surgery < 3 months	2	1,880	48	0.17	Fixed	1.19	0.58 to 2.43	0.64
Sleeping pill use	4	2,351	0	0.99	Fixed	1.81	1.37 to 2.38	< 0.0001
Anti-coagulant or platelet agent	2	1,854	0	0.66	Fixed	1.08	0.74 to 1.58	0.70
Systolic blood pressure	3	2,170	0	0.47	Fixed	2.28	−0.58 to 5.14	0.12
Diastolic blood pressure	3	2,170	49	0.14	Fixed	−0.26	−2.14 to 1.62	0.79
Lower leg varix	2	1,854	0	0.37	Fixed	1.63	1.17 to 2.28	0.004
Lower leg edema	3	2,061	80	0.007	Random	1.00	0.34 to 2.91	1.00
Lower leg pain	2	388	0	0.46	Fixed	0.90	0.31 to 2.57	0.84
Lower leg skin flare	2	1,880	0	0.69	Fixed	1.88	0.58 to 6.04	0.29
Overnight stay in a car	2	471	0	0.90	Fixed	0.93	0.50 to 1.75	0.83
Walking time shortened	3	678	0	0.85	Fixed	1.27	0.79 to 2.02	0.32
Reduced urination	3	2,170	0	0.78	Fixed	0.83	0.61 to 1.12	0.22
Soleal vein dilatation ≥ 8 mm	3	678	49	0.14	Fixed	2.13	1.32 to 3.43	0.002

OR, odds ratio; *MD*, mean difference; *CI*, confidence interval.

Table 4. Sensitivity analysis based on the Newcastle-Ottawa Scale categorized as good and very good studies in terms of quality.

We found that prior history of DVT was significantly associated with DVT. In the included studies, follow-up after DVT diagnosis was short, and the causal relationship remained unknown. However, it has been thought that organized DVT and fresh DVT are strongly associated, and recurrent DVT (especially, soleal vein[58]) indicates a high risk of pulmonary thromboembolism[3,59]. Further investigations into causal relationships between organized DVT and new DVT in the context of Japanese earthquakes are warranted. These investigations should include long-term follow-up or utilization of alternative methods, such as viscoelastic devices[60,61].

DVT was associated not with insomnia itself, but with the use of sleeping pills. Indeed, it has been reported that sleep deprivation is not connected to cardiovascular risks (including DVT risk), except in cases in which individuals consistently receive very little sleep[62]. Furthermore, utilization of sleeping pills has been linked to development of DVT[63]. To provide greater precision, associations with DVT have been observed specifically in cases of newly prescribed benzodiazepine receptor agonists and limited to current prescriptions (≤ 90 days). An explanation to consider is that utilization of benzodiazepine receptor agonists could potentially lead to reduced motor activity, particularly during sleep[64], which in turn may contribute to DVT onset.

Limitations

Several limitations impact the generalizability of the findings from this study. First, study items with slightly variable definitions among studies were consolidated. For instance, the survey periods for DVT vary among studies, from 5 days to 4 years[1–7]. In these studies, within the month following an earthquake, the highest incidence of DVT was around 30% on Day 5. Subsequently, the incidence gradually decreases and remains in the range of 10–19% from four months to four years. Moreover, various earthquakes, i.e., the 2011 Great East Japan earthquake[2,4,6,7] and the 2016 Kumamoto earthquake[1,3,5], have been amalgamated into a single result. The 2011 Great East Japan earthquake struck eastern Japan with a magnitude of 9, followed by a tsunami on March 11, 2011[2,4,6,7]. Subsequent to these occurrences, approximately 470,000 people were estimated to have been evacuated to designated centers[2,4,6,7]. In contrast, the 2016 Kumamoto earthquake struck Kumamoto Prefecture with a magnitude of 6.5 on April 14, 2016 and a magnitude of 7.3 on April 16, followed by over 3,000 aftershocks[1,3,5]. In the aftermath of these events, more than 180,000 individuals are estimated to have been evacuated to designated centers or private vehicles[1,3,5]. The 2011 Great East Japan earthquake transformed public disaster awareness, and prompted changes in disaster response measures following the 2016 Kumamoto earthquake. These changes included establishment of the Health and Medical Coordination Headquarters, followed by the Health, Welfare, and Medical Coordination Headquarters[65]. However, subgroup analyses to investigate potential sources of variation across studies (heterogeneity) were not performed due to the limited number of studies for each factor. Second, the reliability of our findings is dependent upon that of the included studies. Criteria for inclusion were not standardized across the included studies. This variation was partly reflected in the GRADE evaluations. Decision makers, clinicians, and patients should interpret our results based on the quality of evidence. Third, reporting bias may exist according to financial conflicts of interest in two articles[2,7]. Although the funnel plot for the female gender variable (Fig. 2) displayed values within the acceptable range and positioned close to the no-effect line, no statistical assessment, e.g., Begg's or Egger's test, was conducted. Fourth, diagnosis of DVT relied solely on lower leg echo scans, potentially missing cases of proximal DVT. Despite this limitation, focusing on calf DVT remains clinically relevant, as it can serve as a precursor to more serious conditions like proximal DVT and pulmonary embolism. Screening for calf DVT is also practical in post-disaster settings, as it can be conducted while patients are seated and with minimal skin exposure. Early detection and management of calf DVT are crucial for preventing complications. Fifth, the two studies conducted by Onichi et al.[1,3] partially overlapped in terms of the survey period (May 3–4, 2016) and location (Minamiaso Village, Kumamoto Prefecture), which raises the possibility that some subjects may have been included in both studies. This is reflected in the GRADE assessment and should be taken with caution when interpreting our results. Although limitations stemming from the nature of meta-analysis exist, our findings still contribute to informed decision-making regarding healthcare and policy regarding disaster management following earthquakes in Japan.

Conclusions

We synthesized available evidence pertaining to factors associated with DVT following earthquakes in Japan. Importantly, noteworthy factors associated with DVT in this context included female gender, advanced age, hypertension, heart disease, prior history of DVT, use of sleeping pills, lower leg varix, and soleal vein dilatation ≥ 8 mm. While recognizing the constraints in our study, immediate importance of authorities coordinating establishment of prepared shelters and educating evacuees about preventing DVT and PE has been emphasized. Identification of DVT-related factors enables targeted identification of high-risk evacuees at shelters and suggests the potential for effective interventions in preventing DVT in disaster scenarios.

Data availability

All data generated and/or analyzed during the present study are found in the published article.

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Author contributions

YF conceived the study and contributed to data acquisition, drafting, revision, and approval of the final manuscript version. TK conceived the study and contributed to data acquisition, analysis, interpretation, drafting, revision, and approval of the final manuscript version. YF and TK are co-first authors. SN, MK, HK, and YS contributed to critical revision of the article and approved the final version of the manuscript.

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Declarations

Competing interests

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Additional information

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