Supplementary Materials: Association of Plasminogen Activator Inhibitor-1 (*PAI-1*) Gene Polymorphisms with Osteoporotic Vertebral Compression Fractures (OVCFs) in Postmenopausal Women

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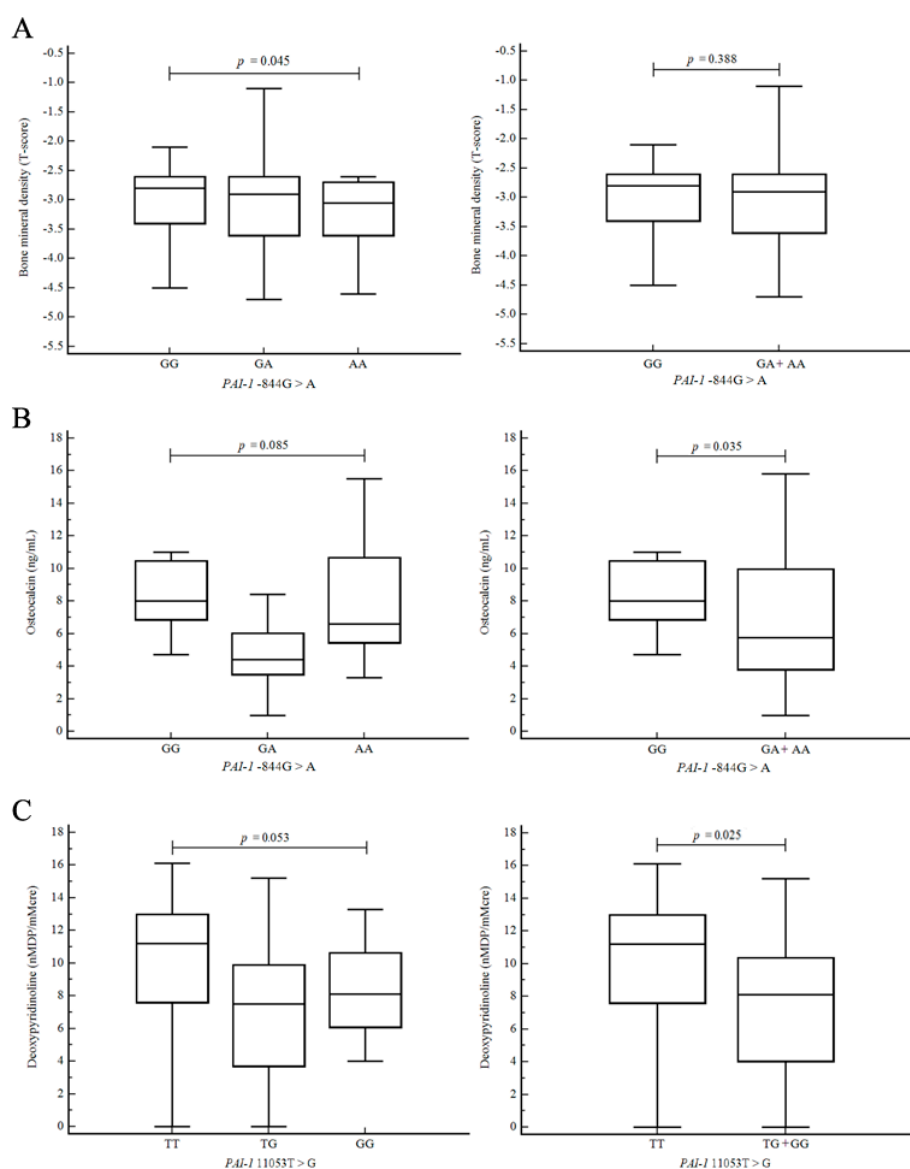
Figure S1. The bone mineral density (BMD), osteocalcin (bone Gla protein, BGP), and deoxypyridinoline (DPD) levels according to *PAI-1* gene polymorphisms in OVCF patients. The statistical analysis was performed by Kruskal-Wallis or Mann-Whitney test for *PAI-1* −844G > A, 11053T > G genotype, respectively. The black line in box was mean of factor value. (**A**) The BMD level: The BMD (*T*-score) of lumbar spine (L2–L4) is significantly different (*p* = 0.045) between PAI-1 −844GG (−3.19 ± 0.84), GA (−2.90 ± 1.01) and AA genotype (−3.44 ± 0.94); (**B**) plasma BGP level: we found that *PAI-1* −844G > A polymorphism is making a difference with plasma BGP level. The *PAI-1* −844GA + AA genotype had a descend osteocalcin level (6.77 ± 3.99) compared with the −844GG genotype (11.78 ± 10.67); (**C**) plasma DPD level: the *PAI-1* 11053TG + GG genotype had a descend DPD level (7.14 ± 4.18) compared with the 11053TT genotype (12.15 ± 7.79).
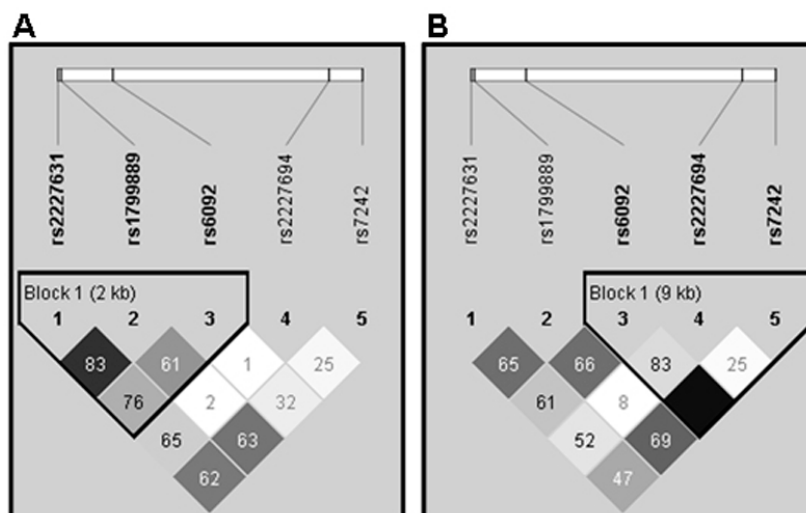
Figure S2. Linkage disequilibrium (LD) patterns of *PAI-1* gene SNPs. Values in squares represent the LD between single markers. The color of area were show "Linkage disequilibrium", that high association with two loci as it gets darker. (**A**) Control individuals exhibited strong linkage disequilibrium between loci −844 and −675 (D′ = 0.838, LOD = 8.42, r^2 = 0.153), −844 and +43 (D′ = 0.764, LOD = 1.2, r^2 = 0.02); (**B**) whereas osteoporosis patients exhibited strong linkage disequilibrium between loci +43 and +11053 (D′ = 1.000, LOD = 4.51, r^2 = 0.106), +43 and +9785 (D′ = 0.831, LOD = 0.06, r^2 = 0.002).

Table S1. Baseline characteristics between OVCF and non-OVCF patients.

Characteristic	OVCF (*n* = 87)	non-OVCF (*n* = 71)	*p*
Age (years, mean ± SD)	70.23 ± 9.44	70.83 ± 6.53	0.846
Hypertension (%)	37 (42.5)	20 (28.2)	0.01
SBP (mmHg, mean ± SD)	129.99 ± 16.51	126.34 ± 13.89	0.183
DBP (mmHg, mean ± SD)	77.63 ± 10.57	74.72 ± 10.26	0.062
Diabetes mellitus (%)	11 (12.6)	17 (23.9)	0.58
FBS (mg/dL, mean ± SD)	135.89 ± 53.96	114.30 ± 26.15	0.003
Hcy (μmol/L, mean ± SD)	10.01 ± 3.85	9.57 ± 4.31	0.499
Folate (ng/mL, mean ± SD)	6.54 ± 4.03	10.19 ± 4.91	<0.0001
BMI (kg/m², mean ± SD)	23.87 ± 5.02	23.77 ± 2.79	0.222
HDL-cholesterol (mg/dL, mean ± SD)	44.39 ± 15.95	44.83 ± 12.24	0.868
LDL-cholesterol (mg/dL, mean ± SD)	117.87 ± 42.82	95.02 ± 32.02	0.002
TG (mg/dL, mean ± SD)	147.62 ± 74.17	132.23 ± 86.68	0.285
Vitamin B12 (pg/mL, mean ± SD)	973.11 ± 1024.37	639.46 ± 384.93	0.028
25-(OH) Vitamin D (ng/mL, mean ± SD)	41.97 ± 34.20	18.57 ± 11.62	<0.0001
Osteocalcin (ng/mL, mean ± SD)	7.83 ± 6.39	-	-
Deoxypyridinoline (nMDP/mMcre, mean ± SD)	8.41 ± 5.55	-	-
BMD (g/cm², mean ± SD)	−2.98 ± 1.26	−3.06 ± 0.97	0.394

Abbreviations: OVCF, osteoporotic vertebral compression fracture; SBP, systolic blood pressure; DBP, diastolic blood pressure; FBS, fasting blood sugar; Hcy, homocysteine; BMI, body mass index; HDL, high density lipoprotein; LDL, low density lipoprotein; TG, triglyceride; BMD, bone mineral density.

Table S2. Comparison of genotype frequencies and AOR values of *PAI-1* polymorphisms according to with/without fracture patients.

Genotypes	non-OVCF (*n* = 71)	OVCF (*n* = 87)	AOR (95% CI) *	*p*
PAI-1 −844	-	-	-	-
GG	22 (31.0)	18 (20.7)	1.000 (reference)	-
GA	33 (46.5)	56 (64.4)	2.456 (1.063–5.676)	0.036
AA	16 (22.5)	13 (14.9)	0.862 (0.274–2.716)	0.800
Dominant (GG vs. GA + AA)	-	-	1.884 (0.848–4.183)	0.120
Recessive (GG + GA vs. AA)	-	-	0.431 (0.170–1.094)	0.077
PAI-1 −675 4G5G	-	-	-	-
4G4G	33 (46.5)	36 (41.4)	-	-
4G5G	32 (45.1)	38 (43.7)	1.084 (0.527–2.230)	0.827
5G5G	6 (8.5)	13 (14.9)	1.578 (0.490–5.082)	0.444
Dominant (4G4G vs. 4G5G + 5G5G)	-	-	1.207 (0.610–2.389)	0.589
Recessive (4G4G + 4G5G vs. 5G5G)	-	-	1.614 (0.535–4.869)	0.395
PAI-1 +43	-	-	-	-
GG	61 (85.9)	71 (81.6)	-	-
GA	8 (11.3)	16 (18.4)	1.599 (0.589–4.341)	0.357
AA	2 (2.8)	0 (0.0)	N/A	0.998
Dominant (GG vs. GA + AA)	-	-	1.286 (0.500–3.303)	0.602
Recessive (GG + GA vs. AA)	-	-	N/A	0.998
PAI-1 +9785	-	-	-	-
GG	68 (95.8)	80 (92.0)	-	-
GA	3 (4.2)	7 (8.0)	1.675 (0.385–7.293)	0.492
AA	0 (0.0)	0 (0.0)	N/A	-
Dominant (GG vs. GA + AA)	-	-	1.675 (0.385–7.293)	0.492
Recessive (GG + GA vs. AA)	-	-	N/A	-
PAI-1 +11053	-	-	-	-
TT	15 (21.1)	18 (20.7)	-	-
TG	36 (50.7)	49 (56.3)	1.316 (0.534–3.246)	0.551
GG	20 (28.2)	20 (23.0)	0.916 (0.326–2.575)	0.868
Dominant (TT vs. TG + GG)	-	-	1.148 (0.494–2.666)	0.748
Recessive (TT + TG vs. GG)	-	-	0.803 (0.373–1.728)	0.575

* The adjusted odds ratio on the basis of risk factors, such as age, hypertension, diabetes mellitus.

Abbreviations: AOR, adjusted odds ratio; N/A, not applicable.

Table S3. Comparison of genotype frequencies of the *PAI-1* gene 4 site haplotype in the context of OVCF in postmenopausal women and control subjects.

Haplotype	Overall (2*n* = 710)	Control (2*n* = 394)	Case (2*n* = 316)	OR (95% CI)	*p* [a]
PAI-1 −844/−675/+43/+9785			-	-	-
G-4G-G-G	0.274	0.332	0.194	1.000 (reference)	-
G-4G-G-A	0.011	0.024	0.000	0.102 (0.006–1.767)	0.034
G-4G-A-G	0.028	0.010	0.052	9.127 (2.945–28.28)	<0.0001
G-4G-A-A	0.005	0.000	0.008	10.69 (0.505–226.2)	0.104
G-5G-G-G	0.189	0.180	0.208	1.996 (1.270–3.139)	0.003
G-5G-G-A	0.008	0.008	0.000	0.306 (0.016–6.010)	0.553
G-5G-A-G	0.049	0.029	0.074	4.116 (1.922–8.814)	0.000
G-5G-A-A	0.000	0.003	0.000	0.713 (0.029–17.76)	1.000
A-4G-G-G	0.366	0.388	0.339	1.502 (1.015–2.222)	0.049
A-4G-G-A	0.011	0.006	0.021	7.516 (1.516–37.26)	0.008
A-4G-A-G	0.022	0.004	0.045	15.03 (3.312–68.24)	<0.0001
A-5G-G-G	0.021	0.016	0.027	2.863 (0.952–8.615)	0.076
A-5G-A-G	0.015	0.000	0.031	44.90 (2.587–779.3)	<0.0001
A-5G-A-A	0.001	0.000	0.003	6.415 (0.257–159.9)	0.321
PAI-1 −844/−675/+43/+11053			-	-	-
G-4G-G-T	0.187	0.256	0.100	1.000 (reference)	-
G-4G-G-G	0.098	0.106	0.093	2.179 (1.174–4.044)	0.016
G-4G-A-T	0.015	0.000	0.035	71.83 (4.115–1254)	<0.0001
G-4G-A-G	0.016	0.006	0.025	8.417 (2.106–33.64)	0.002
G-5G-G-T	0.166	0.163	0.169	2.614 (1.524–4.482)	0.001
G-5G-G-G	0.031	0.022	0.039	4.208 (1.625–10.90)	0.004
G-5G-A-T	0.041	0.030	0.061	4.997 (2.190–11.40)	0.0002
G-5G-A-G	0.009	0.003	0.014	12.63 (1.361–117.1)	0.017
A-4G-G-T	0.069	0.079	0.061	1.934 (0.965–3.880)	0.067
A-4G-G-G	0.308	0.311	0.300	2.458 (1.521–3.971)	0.0002
A-4G-A-T	0.003	0.003	0.000	1.041 (0.041–26.20)	1.000
A-4G-A-G	0.020	0.003	0.045	44.19 (5.588–349.4)	<0.0001
A-5G-G-T	0.010	0.000	0.020	40.60 (2.225–740.9)	0.0000
A-5G-G-G	0.011	0.018	0.006	0.902 (0.178–4.563)	1.000
A-5G-A-T	0.015	0.000	0.033	65.58 (3.737–1151)	<0.0001
PAI-1 −844/−675/+9785/+11053			-	-	-
G-4G-G-T	0.190	0.235	0.132	1.000 (reference)	-
G-4G-G-G	0.108	0.107	0.121	2.003 (1.132–3.544)	0.020
G-4G-A-T	0.012	0.019	0.000	0.147 (0.008–2.629)	0.105
G-4G-A-G	0.007	0.007	0.002	0.314 (0.016–6.225)	0.553
G-5G-G-T	0.197	0.185	0.228	2.184 (1.340–3.560)	0.002
G-5G-G-G	0.039	0.021	0.049	4.429 (1.758–11.16)	0.002
G-5G-A-T	0.010	0.009	0.000	0.314 (0.016–6.225)	0.553
G-5G-A-G	0.003	0.003	0.003	2.214 (0.135–36.28)	0.531
A-4G-G-T	0.067	0.080	0.056	1.286 (0.648–2.553)	0.482
A-4G-G-G	0.329	0.313	0.324	1.836 (1.172–2.877)	0.008
A-4G-A-T	0.006	0.003	0.007	4.429 (0.370–50.23)	0.238
A-4G-A-G	0.000	0.000	0.016	24.20 (1.307–448.0)	0.004
A-5G-G-T	0.027	0.000	0.051	72.60 (4.252–1239)	<0.0001
A-5G-G-G	0.009	0.018	0.007	0.633 (0.126–3.176)	0.722
A-5G-A-T	0.000	0.000	0.004	6.600 (0.263–165.5)	0.316

Table S3. *Cont.*

Haplotype	Overall (2*n* = 710)	Control (2*n* = 394)	Case (2*n* = 316)	OR (95% CI)	*p* [a]
PAI-1 −844/+43/+9785/+11053			-	-	-
G-G-G-T	0.339	0.391	0.266	1.000 (reference)	-
G-G-G-G	0.122	0.118	0.135	1.677 (1.026–2.743)	0.043
G-G-A-T	0.017	0.025	0.000	0.087 (0.005–1.505)	0.018
G-G-A-G	0.007	0.010	0.000	0.203 (0.011–3.822)	0.301
G-A-G-T	0.047	0.029	0.090	4.667 (2.212–9.846)	<0.0001
G-A-G-G	0.027	0.011	0.041	5.958 (1.883–18.86)	0.001
G-A-A-T	0.005	0.003	0.000	0.610 (0.025–15.14)	1.000
G-A-A-G	0.002	0.000	0.004	5.485 (0.221–136.2)	0.356
A-G-G-T	0.074	0.080	0.077	1.375 (0.760–2.486)	0.355
A-G-G-G	0.316	0.327	0.287	1.293 (0.886–1.887)	0.211
A-G-A-T	0.005	0.003	0.004	1.833 (0.113–29.71)	1.000
A-G-A-G	0.002	0.000	0.019	23.77 (1.322–427.4)	0.002
A-A-G-T	0.021	0.000	0.037	45.71 (2.671–782.2)	<0.0001
A-A-G-G	0.019	0.004	0.037	22.00 (2.810–172.2)	<0.0001
A-A-A-T	0.000	0.000	0.005	5.485 (0.221–136.2)	0.356
PAI-1 −675/+43/+9785/+11053			-	-	-
4G-G-G-T	0.243	0.313	0.155	1.000 (reference)	-
4G-G-G-G	0.393	0.408	0.373	1.840 (1.224–2.766)	0.004
4G-G-A-T	0.013	0.018	0.001	0.166 (0.009–2.970)	0.192
4G-G-A-G	0.012	0.012	0.020	3.012 (0.878–10.33)	0.090
4G-A-G-T	0.017	0.004	0.036	27.61 (3.470–219.8)	<0.0001
4G-A-G-G	0.037	0.010	0.070	13.81 (4.523–42.14)	<0.0001
4G-A-A-T	0.002	0.000	0.004	7.485 (0.300–187.0)	0.289
5G-G-G-T	0.170	0.161	0.189	2.391 (1.473–3.881)	0.001
5G-G-G-G	0.043	0.035	0.050	2.896 (1.302–6.322)	0.011
5G-G-A-T	0.005	0.006	0.000	0.499 (0.024–10.59)	1.000
5G-G-A-G	0.001	0.003	0.000	0.832 (0.033–20.78)	1.000
5G-A-G-T	0.055	0.027	0.090	6.390 (2.952–13.83)	<0.0001
5G-A-G-G	0.006	0.003	0.006	5.020 (0.445–56.67)	0.204
5G-A-A-T	0.003	0.003	0.003	2.510 (0.154–40.96)	0.493
5G-A-A-G	0.001	0.000	0.003	7.485 (0.300–187.0)	0.289

[a] Fisher's exact test.

Table S4. Comparison of genotype frequencies of the *PAI-1* gene 3 site haplotype in the context of OVCF in postmenopausal women and control subjects.

Haplotype	Overall (2*n* = 710)	Control (2*n* = 394)	Case (2*n* = 316)	OR (95% CI)	*p* [a]
PAI-1 −844/−675/+43	-	-	-	-	-
G-4G-G	0.287	0.356	0.196	1.000 (reference)	-
G-4G-A	0.032	0.010	0.059	10.73 (3.502–32.85)	<0.0001
G-5G-G	0.197	0.188	0.207	2.014 (1.288–3.148)	0.002
G-5G-A	0.048	0.032	0.072	3.995 (1.900–8.399)	0.0002
A-4G-G	0.376	0.394	0.358	1.646 (1.120–2.419)	0.012
A-4G-A	0.022	0.004	0.045	15.81 (3.485–71.68)	<0.0001
A-5G-G	0.021	0.016	0.027	3.387 (1.155–9.931)	0.042
A-5G-A	0.017	0.000	0.035	51.70 (2.997–891.9)	<0.0001
PAI-1 −844/−675/+9785	-	-	-	-	-
G-4G-G	0.303	0.342	0.252	1.000 (reference)	-
G-4G-A	0.016	0.024	0.006	0.375 (0.079–1.780)	0.335
G-5G-G	0.235	0.209	0.275	1.790 (1.189–2.696)	0.007
G-5G-A	0.009	0.011	0.002	0.422 (0.046–3.843)	0.654
A-4G-G	0.387	0.392	0.381	1.315 (0.913–1.895)	0.165
A-4G-A	0.011	0.006	0.020	5.063 (0.994–25.69)	0.057
A-5G-G	0.039	0.016	0.060	5.344 (2.048–13.94)	0.0002
A-5G-A	0.001	0.000	0.004	5.050 (0.203–125.5)	0.375
PAI-1 −844/−675/+11053	-	-	-	-	-
G-4G-T	0.202	0.254	0.133	1.000 (reference)	-
G-4G-G	0.114	0.114	0.121	2.011 (1.146–3.529)	0.021
G-5G-T	0.206	0.194	0.228	2.256 (1.391–3.659)	0.001
G-5G-G	0.041	0.024	0.053	4.048 (1.712–9.569)	0.002
A-4G-T	0.072	0.083	0.062	1.443 (0.744–2.798)	0.302
A-4G-G	0.329	0.313	0.342	2.091 (1.342–3.258)	0.001
A-5G-T	0.027	0.000	0.054	82.76 (4.862–1409)	<0.0001
A-5G-G	0.009	0.018	0.007	0.680 (0.136–3.412)	1.000
PAI-1 −844/+43/+9785	-	-	-	-	-
G-G-G	0.464	0.513	0.402	1.000 (reference)	-
G-G-A	0.020	0.032	0.000	0.059 (0.003–0.999)	0.003
G-A-G	0.074	0.039	0.123	4.135 (2.190–7.809)	<0.0001
G-A-A	0.006	0.003	0.010	4.772 (0.491–46.40)	0.303
A-G-G	0.386	0.403	0.365	1.150 (0.830–1.595)	0.406
A-G-A	0.011	0.006	0.022	5.567 (1.138–27.23)	0.032
A-A-G	0.040	0.005	0.079	19.88 (4.628–85.41)	<0.0001
PAI-1 −844/+43/+9785	-	-	-	-	-
G-G-T	0.355	0.416	0.269	1.000 (reference)	-
G-G-G	0.129	0.128	0.132	1.589 (0.978–2.581)	0.078
G-A-T	0.052	0.031	0.084	4.341 (2.094–8.988)	<0.0001
G-A-G	0.028	0.010	0.049	7.718 (2.501–23.82)	0.0002
A-G-T	0.079	0.083	0.080	1.462 (0.817–2.616)	0.225
A-G-G	0.318	0.327	0.307	1.451 (1.001–2.104)	0.059
A-A-T	0.021	0.000	0.045	55.80 (3.286–947.3)	<0.0001
A-A-G	0.019	0.004	0.034	21.22 (2.693–167.2)	<0.0001
PAI-1 −844/+9785/+11053	-	-	-	-	-
G-G-T	0.388	0.420	0.357	1.000 (reference)	-
G-G-G	0.146	0.129	0.172	1.546 (0.984–2.428)	0.065
G-A-T	0.021	0.028	0.000	0.063 (0.004–1.087)	0.004
G-A-G	0.009	0.010	0.006	0.730 (0.131–4.055)	1.000
A-G-T	0.092	0.080	0.109	1.551 (0.905–2.659)	0.128
A-G-G	0.338	0.331	0.331	1.179 (0.830–1.676)	0.371
A-A-T	0.007	0.003	0.012	5.841 (0.644–52.97)	0.164
A-A-G	0.000	0.000	0.013	13.12 (0.699–246.3)	0.029

Table S4. *Cont.*

Haplotype	Overall (2*n* = 710)	Control (2*n* = 394)	Case (2*n* = 316)	OR (95% CI)	*p* [a]
PAI-1 −675/+43/+9785	-	-	-	-	-
4G-G-G	0.637	0.720	0.529	1.000 (reference)	-
4G-G-A	0.026	0.031	0.022	0.992 (0.383–2.570)	1.000
4G-A-G	0.052	0.014	0.102	10.88 (4.159–28.48)	<0.0001
4G-A-A	0.002	0.000	0.005	8.493 (0.401–178.1)	0.139
5G-G-G	0.212	0.197	0.237	1.656 (1.143–2.401)	0.010
5G-G-A	0.005	0.007	0.000	0.243 (0.012–4.730)	0.301
5G-A-G	0.062	0.030	0.100	4.535 (2.273–9.047)	<0.0001
5G-A-A	0.003	0.003	0.005	1.701 (0.106–27.39)	1.000
PAI-1 −675/+9785/+11053	-	-	-	-	-
4G-G-T	0.257	0.331	0.159	1.000 (reference)	-
4G-G-G	0.405	0.419	0.394	1.969 (1.319–2.939)	0.001
4G-A-T	0.018	0.004	0.038	31.44 (3.982–248.3)	<0.0001
4G-A-G	0.037	0.010	0.068	13.76 (4.497–42.08)	<0.0001
5G-G-T	0.176	0.166	0.189	2.418 (1.498–3.904)	0.0002
5G-G-G	0.042	0.038	0.046	2.620 (1.193–5.753)	0.019
5G-A-T	0.057	0.030	0.092	6.332 (2.998–13.37)	<0.0001
5G-A-G	0.009	0.003	0.014	10.48 (1.143–96.10)	0.026
PAI-1 +43/+9785/+11053	-	-	-	-	-
G-G-T	0.417	0.476	0.348	1.000 (reference)	-
G-G-G	0.432	0.440	0.418	1.304 (0.941–1.808)	0.115
G-A-T	0.017	0.023	0.000	0.090 (0.005–1.559)	0.029
G-A-G	0.014	0.015	0.022	1.994 (0.653–6.085)	0.249
A-G-T	0.069	0.028	0.124	6.060 (2.981–12.32)	<0.0001
A-G-G	0.045	0.015	0.078	7.121 (2.833–17.90)	<0.0001
A-A-T	0.004	0.003	0.005	3.418 (0.306–38.16)	0.558
A-A-G	0.002	0.000	0.005	8.529 (0.406–179.4)	0.139

[a] Fisher's exact test.

Table S5. Comparison of genotype frequencies of the *PAI-1* gene 2 site haplotype in the context OVCF in postmenopausal women and control subjects.

Haplotype	Overall (2*n* = 710)	Control (2*n* = 394)	Case (2*n* = 316)	OR (95% CI)	*p* [a]
PAI-1 −844/−675	-	-	-	-	-
G-4G	0.319	0.366	0.258	1.000 (reference)	-
G-5G	0.244	0.22	0.277	1.798 (1.202–2.689)	0.004
A-4G	0.398	0.398	0.401	1.438 (1.004–2.059)	0.057
A-5G	0.039	0.016	0.065	5.926 (2.287–15.36)	<0.0001
PAI-1 −844/+43	-	-	-	-	-
G-G	0.483	0.545	0.402	1.000 (reference)	-
G-A	0.08	0.041	0.133	4.444 (2.399–8.231)	<0.0001
A-G	0.397	0.409	0.386	1.283 (0.930–1.770)	0.14
A-A	0.039	0.005	0.079	21.16 (4.928–90.87)	<0.0001
PAI-1 −844/+9785	-	-	-	-	-
G-G	0.538	0.552	0.527	1.000 (reference)	-
G-A	0.025	0.035	0.008	0.280 (0.079–0.991)	0.044
A-G	0.425	0.408	0.442	1.137 (0.839–1.540)	0.439
A-A	0.011	0.006	0.024	4.575 (0.938–22.32)	0.048
PAI-1 −844/+11053	-	-	-	-	-
G-T	0.409	0.448	0.359	1.000 (reference)	-
G-G	0.154	0.139	0.175	1.544 (0.992–2.402)	0.055
A-T	0.098	0.083	0.119	1.731 (1.024–2.927)	0.044
A-G	0.339	0.331	0.347	1.306 (0.924–1.847)	0.134
PAI-1 −675/+43	-	-	-	-	-
4G-G	0.663	0.75	0.552	1.000 (reference)	-
4G-A	0.054	0.014	0.106	11.57 (4.440–30.14)	<0.0001
5G-G	0.218	0.204	0.236	1.595 (1.105–2.301)	0.014
5G-A	0.066	0.032	0.106	4.318 (2.213–8.428)	<0.0001
PAI-1 −675/+9785	-	-	-	-	-
4G-G	0.69	0.734	0.635	1.000 (reference)	-
4G-A	0.027	0.03	0.023	0.839 (0.325–2.168)	0.815
5G-G	0.274	0.226	0.334	1.696 (1.213–2.371)	0.002
5G-A	0.01	0.011	0.008	1.078 (0.239–4.872)	1
PAI-1 −675/+11053	-	-	-	-	-
4G-T	0.274	0.334	0.197	1.000 (reference)	-
4G-G	0.443	0.43	0.462	1.839 (1.265–2.675)	0.002
5G-T	0.233	0.196	0.281	2.461 (1.602–3.780)	<0.0001
5G-G	0.05	0.04	0.061	2.528 (1.218–5.249)	0.013
PAI-1 +43/+9785	-	-	-	-	-
G-G	0.85	0.916	0.767	1.000 (reference)	-
G-A	0.031	0.038	0.021	0.696 (0.280–1.733)	0.511
A-G	0.114	0.043	0.202	5.616 (3.211–9.823)	<0.0001
A-A	0.006	0.003	0.011	4.475 (0.463–43.30)	0.308
PAI-1 +43/+11053	-	-	-	-	-
G-T	0.434	0.499	0.348	1.000 (reference)	-
G-G	0.446	0.455	0.44	1.391 (1.008–1.919)	0.05
A-T	0.073	0.031	0.13	6.119 (3.086–12.13)	<0.0001
A-G	0.047	0.014	0.082	7.761 (3.099–19.44)	<0.0001
PAI-1 +9785/+11053	-	-	-	-	-
G-T	0.486	0.504	0.466	1.000 (reference)	-
G-G	0.478	0.455	0.502	1.202 (0.889–1.626)	0.249
A-T	0.021	0.026	0.012	0.542 (0.167–1.761)	0.411
A-G	0.015	0.014	0.02	1.354 (0.428–4.283)	0.768

[a] Fisher's exact test.

Table S6. Stratified analysis of *PAI-1* polymorphisms for hypertension, diabetes mellitus, 25-OH vit. D, vit. B$_{12}$, folate, and homocysteine levels.

Characteristics	*PAI-1* −844 GA + AA		*PAI-1* −675 5G5G		*PAI-1* 43 GA + AA		*PAI-1* 9785 GA + AA		*PAI-1* 11053 TG + GG	
	AOR (95% CI) *	*p*	AOR (95% CI) *	*p*	AOR (95% CI) *	*p*	AOR (95% CI) *	*p*	AOR (95% CI) *	*p*
Hypertension (−)	2.057 (1.053–4.019)	0.035	1.156 (0.326–4.098)	0.822	2.664 (0.977–7.260)	0.056	0.708 (0.196–2.563)	0.599	1.127 (0.564–2.254)	0.735
Hypertension (+)	1.097 (0.528–2.276)	0.804	8.013 (1.906–33.69)	0.005	1.555 (0.550–4.398)	0.405	1.467 (0.428–5.036)	0.542	1.858 (0.803–4.299)	0.148
Diabetes mellitus (−)	1.721 (1.010–2.932)	0.046	5.058 (1.655–15.46)	0.005	2.050 (0.954–4.406)	0.066	0.916 (0.364–2.304)	0.852	1.303 (0.745–2.280)	0.354
Diabetes mellitus (+)	0.883 (0.231–3.374)	0.856	0.589 (0.082–4.214)	0.598	1.620 (0.217–12.090)	0.638	8.208 (0.264–255.001)	0.23	2.849 (0.502–16.185)	0.237
25-OH vit. D ≥ 30 ng/mL	0.440 (0.108–1.791)	0.252	19.126 (0.998–366.8)	0.05	2.910 (0.510–16.618)	0.23	N/A	0.998	0.664 (0.148–2.978)	0.592
25-OH vit. D < 30 ng/mL	1.643 (0.780–3.461)	0.192	1.208 (0.200–7.306)	0.837	0.853 (0.272–2.680)	0.786	0.825 (0.169–4.020)	0.812	1.245 (0.563–2.751)	0.589
Vit. B$_{12}$ > 400 pg/mL	1.314 (0.650–2.654)	0.447	1.800 (0.403–8.039)	0.441	1.968 (0.772–5.017)	0.156	0.339 (0.042–2.737)	0.31	1.113 (0.519–2.387)	0.784
Vit. B$_{12}$ ≤ 400 pg/mL	1.042 (0.410–2.652)	0.931	3.604 (0.590–22.04)	0.165	1.249 (0.309–5.039)	0.755	1.930 (0.383–9.727)	0.425	1.187 (0.403–3.490)	0.756
Folate > 4.40 nmol/L [a]	1.774 (1.016–3.096)	0.044	2.397 (0.876–6.558)	0.089	1.737 (0.802–3.762)	0.162	0.706 (0.243–2.050)	0.522	1.476 (0.818–2.665)	0.196
Folate ≤ 4.40 nmol/L [a]	1.230 (0.310–4.885)	0.768	N/A	N/A	7.406 (0.716–76.644)	0.093	N/A	N/A	0.933 (0.207–4.210)	0.928
tHcy < 12.41 μmol/L [b]	1.512 (0.393–5.822)	0.548	5.543 (0.566–54.29)	0.141	1.812 (0.842–3.900)	0.128	1.794 (0.145–22.18)	0.649	0.670 (0.150–2.991)	0.599
tHcy ≥ 12.41 μmol/L [b]	1.590 (0.929–2.720)	0.091	2.394 (0.839–6.832)	0.103	5.133 (0.513–51.334)	0.164	0.860 (0.312–2.369)	0.77	1.581 (0.884–2.829)	0.123

* 95% CI indicates 95% confidence interval. Adjusted by age, hypertension, diabetes mellitus; [a] 4.40 nmol/L is based on the bottom 15% of the folate level in patients and control group; [b] 12.41 μmol/L is based on the top. Abbreviations: AOR, adjusted odds ratio; N/A, not applicable.

Table S7. Combined effects of *PAI-1* genotype and homocysteine and folate levels on OVCF risk in postmenopausal women.

Genotypes	Folate > 4.40 nmol/L [a]	Folate ≤ 4.40 nmol/L [a]	tHcy < 12.41 μmol/L [b]	tHcy ≥ 12.41 μmol/L [b]
PAI-1 −844 GG	1.000 (reference)	3.091 (0.903–10.580)	1.000 (reference)	1.972 (0.587–6.628)
PAI-1 −844 GA + AA	1.774 (1.016–3.096)	2.784 (1.172–6.613)	1.590 (0.929–2.720)	2.522 (1.074–5.921)
PAI-1 −675 4G4G	1.000 (reference)	1.627 (0.591–4.481)	1.000 (reference)	1.394 (0.590–3.295)
PAI-1 −675 4G5G + 5G5G	1.615 (0.981–2.660)	3.625 (1.404–9.362)	1.631 (0.994–2.674)	3.571 (1.212–10.52)
PAI-1 43 GG	1.000 (reference)	1.456 (0.716–2.960)	1.000 (reference)	1.812 (0.842–3.900)
PAI-1 43 GA + AA	1.737 (0.802–3.762)	9.247 (1.049–81.51)	1.450 (0.741–2.834)	8.000 (0.865–73.99)
PAI-1 9785 GG	1.000 (reference)	1.617 (0.816–3.203)	1.000 (reference)	1.608 (0.835–3.095)
PAI-1 9785 GA + AA	0.706 (0.243–2.050)	N/A	0.860 (0.312–2.369)	2.780 (0.237–32.58)
PAI-1 11053 TT	1.000 (reference)	2.607 (0.591–11.49)	1.000 (reference)	3.598 (0.873–14.83)
PAI-1 11053 TG + GG	1.476 (0.818–2.665)	2.468 (1.035–5.887)	1.581 (0.884–2.829)	2.275 (0.952–5.440)

[a] 4.40 nmol/L is based on the bottom 15% folate level in patients and control group; [b] 12.41 μmol/L is based on the top 15% homocysteine level in patients and control group. Abbreviations: N/A, not applicable.

Table S8. The BMD, vit. B12, 25-OH vit. D, osteocalcin, and DPD levels according to *PAI-1* gene polymorphisms in OVCF patients.

Genotypes	BMD (g/cm2)		Vit. B12 (pmol/L)		25-Vit. D (ng/mL)		Osteocalcin (ng/mL)		DPD (nMDP/mMcre)	
	Mean ± SD	CV (%)	Mean ± SD	CV (%)	Mean ± SD	CV (%)	Mean ± SD	CV (%)	Mean ± SD	CV (%)
PAI-1 −844	-	-	-	-	-	-	-	-	-	-
GG	−3.19 ± 0.84	26.3	720.12 ± 668.90	92.9	28.23 ± 26.10	92.5	11.78 ± 10.67	90.6	7.15 ± 5.14	71.9
GA	−2.90 ± 1.01	34.8	798.06 ± 894.35	112.1	25.42 ± 21.08	82.9	6.34 ± 3.91	61.7	7.68 ± 4.59	59.8
AA	−3.44 ± 0.94	27.3	717.77 ± 368.68	51.4	14.67 ± 11.65	79.4	8.27 ± 4.19	50.7	11.92 ± 8.14	68.3
p	0.045	-	0.688	-	0.15	-	0.085	-	0.207	-
GG vs. GA + AA	−3.02 ± 1.01	33.4	774.47 ± 777.35	100.4	22.32 ± 19.37	86.8	6.77 ± 3.99	58.9	8.62 ± 5.67	65.8
p	0.388	-	0.571	-	0.291	-	0.035 *	-	0.516	-
PAI-1 −675	-	-	-	-	-	-	-	-	-	-
4G4G	−3.03 ± 0.84	27.7	707.41 ± 477.10	67.4	20.86 ± 22.43	107.5	10.30 ± 8.96	87	7.50 ± 4.44	59.2
4G5G	−3.12 ± 1.08	34.6	787.06 ± 861.90	109.5	25.88 ± 21.17	81.8	6.59 ± 3.56	54	7.62 ± 4.91	64.4
5G5G	−2.95 ± 0.97	32.9	1041.54 ± 1634.34	156.9	32.83 ± 16.14	49.2	6.05 ± 3.69	61	13.85 ± 9.11	65.8
p	0.772	-	0.254	-	0.406	-	0.177	-	0.098	-
4G4G vs. 4G5G + 5G5G	−3.09 ± 1.05	34.0	814.18 ± 966.52	118.7	26.77 ± 20.55	76.8	6.46 ± 3.53	54.6	8.75 ± 6.12	69.9
p	0.72	-	0.241	-	0.244	-	0.062	-	0.525	-
PAI-1 +43	-	-	-	-	-	-	-	-	-	-
GG	−3.07 ± 0.99	32.2	761.07 ± 772.88	101.6	23.47 ± 21.97	93.6	7.98 ± 6.73	84.3	8.42 ± 4.01	47.6
GA	−3.10 ± 0.90	29.0	745.63 ± 362.05	48.6	28.93 ± 20.88	72.2	7.34 ± 2.19	29.8	7.50 ± 11.88	158.4
AA	−2.50 ± 0.00	0.0	433.33 ± 221.67	51.2	21.58 ± 9.79	45.4	-	-	-	-
p	0.709	-	0.748	-	0.79	-	0.835	-	0.736	-
GG vs. GA + AA	−3.04 ± 0.88	28.9	710.93 ± 360.20	50.7	27.46 ± 18.96	69	7.34 ± 2.19	29.8	7.50 ± 11.88	158.4
p	0.906	-	0.74	-	0.589	-	0.835	-	0.736	-
PAI-1 +9785	-	-	-	-	-	-	-	-	-	-
GG	−3.05 ± 0.92	30.2	762.75 ± 763.15	100.1	24.39 ± 21.69	88.9	7.83 ± 6.30	80.5	8.28 ± 5.67	68.5
GA	−3.24 ± 1.58	48.8	664.53 ± 317.31	47.7	10.80 ± 0.01	0.1	9.20 ± 9.33	101.4	8.30 ± 2.26	27.2
AA	-	-	627	-	-	-	-	-	-	-
p	0.564	-	0.857	-	0.382	-	0.77	-	0.997	-
GG vs. GA + AA	−3.24 ± 1.58	48.8	662.44 ± 307.96	46.5	10.80 ± 0.01	0.1	9.20 ± 9.33	101.4	8.30 ± 2.26	27.2
p	0.564	-	0.58	-	0.382	-	0.77	-	0.997	-

Table S8. *Cont.*

Genotypes	BMD (g/cm2)		Vit. B$_{12}$ (pmol/L)		25-Vit. D (ng/mL)		Osteocalcin (ng/mL)		DPD (nMDP/mMcre)	
	Mean ± SD	CV (%)	Mean ± SD	CV (%)	Mean ± SD	CV (%)	Mean ± SD	CV (%)	Mean ± SD	CV (%)
PAI-1 +11053	-	-	-	-	-	-	-	-	-	-
TT	−3.27 ± 0.88	26.9	777.10 ± 751.91	96.8	25.49 ± 15.97	62.7	5.91 ± 2.84	48.1	12.15 ± 7.79	64.1
TG	−2.99 ± 0.98	32.8	684.05 ± 485.48	71	23.90 ± 24.69	103.3	8.92 ± 8.47	95	6.54 ± 4.56	69.7
GG	−3.07 ± 1.01	32.9	891.56 ± 1104.54	123.9	23.06 ± 19.83	86	8.14 ± 3.72	45.7	8.33 ± 3.20	38.4
p	0.464	-	0.181	-	0.945	-	0.46	-	0.053	-
TT vs. TG + GG	−3.02 ± 0.99	32.8	748.70 ± 739.61	98.8	23.60 ± 22.92	97.1	8.66 ± 7.12	82.2	7.14 ± 4.18	58.5
p	0.234	-	0.785	-	0.759	-	0.225	-	0.022	-

Note: BMD, bone mineral density; Vit. B$_{12}$, plasma vitamin B$_{12}$; 25-Vit. D, 25-OH (hydroxyl) vitamin D; DPD, Deoxypyridinoline; SD, standard deviation; CV, between-person coefficient of variation; * Analysis was performed by Kruskal–Wallis test in the differences of biochemical parameters between *PAI-1* gene polymorphisms in OVCF women.

Table S9. The polymerase chain reaction (PCR) restriction fragment length polymorphism (RFLP) assay.

SNPs	Polymorphism	Region	rs #	Forward Primer (5′-3′)	Reverse Primer (5′-3′)	Restriction Enzyme *
PAI-1 −844	G > A	5′-UTR	rs2227631	5′-CAG GCT CCC ACT GAT TCT AC-3′	5′-GAG GGC TCT CTT GTG TCA AC-3′	*Xho* I
PAI-1 −675	4G > 5G	5′-UTR	rs1799889	5′-CCA ACA GAG GAC TCT TGG TC-3′	5′-CAC AGA GAG AGT CTG GCC ACG-3′	*Bsl* I
PAI-1 +43	G > A	Exon 2	rs6092	5′-TGT CTT CCA GAA CGA TTC CTT CAC C-3′	5′-GTT GTC AGC TGG AGC ATG GCC-3′	*PshA* I
PAI-1 +9785	G > A	Intron 7	rs2227694	5′-TTA GCC AGG CAT GGT GGC ATG-3′	5′-CGG GCT GAG ACT ATG ACA GCT GC-3′	*Aci* I
PAI-1 +11053	T > G	3′-UTR	rs7242	5′-GCT GGG CAC GCA TCT GGC-3′	5′-TCT CCC TCC CCA GAA ACA GTG TGC-3′	*Hae* III

* All of the restriction enzymes were available from New England Biolabs (MA, USA) and we used the reaction conditions recommended by the instructions.