

Supplemental Table 1. Rabbits examined in this study

	10-16 months old		17-22 months old		23-29 months old		Total	
	Females	Males	Females	Males	Females	Males	Females	Males
Sacrificed rabbits	26	37	15	16	8	5	49	58
Sudden death	20	1	18	8	26	7	64	16
Total	46	38	33	24	34	12	113	74
% of sudden death	43.5%	2.6%	54.5%	33.3%	76.5%	58.3%	56.6%	21.6%
Fisher's exact probability test	<i>P</i> <0.001		<i>P</i> =0.178		<i>P</i> =0.276		<i>P</i> <0.001	

The frequency of rabbits that died suddenly (females + males) was significantly increased with aging (*P*=0.008) according to the Cochran-Mantel-Haenszel test, although the age-related increase in the frequency was not statistically significant in analysis using either only females or males when analyzed independently.

Supplemental Table 2. Gender differences in degree of coronary lesions

Months old	Frequency of sections with lesion (%)			Frequency of sections with >75% stenosis (%)			Maximum stenosis (%)		
	10-16	17-22	23-29	10-16	17-22	23-29	10-16	17-22	23-29
Rabbits that had died suddenly									
Female	81 ± 4.3	91 ± 2.9	85 ± 2.6	54 ± 4.8	67 ± 2.9	61 ± 3.0	94 ± 0.8	95 ± 0.0	94 ± 0.3
Male	81	95 ± 2.0	95 ± 2.2	37	69 ± 3.8	71 ± 6.6	95	95 ± 0.0	94 ± 0.9
		<i>P=0.501</i>	<i>P=0.067</i>		<i>P=1.000</i>	<i>P=0.226</i>		<i>ns</i>	<i>P=0.272</i>
Rabbits sacrificed									
Female	60 ± 5.7	76 ± 3.9	73 ± 8.0	26 ± 6.4	29 ± 5.6	44 ± 9.5	75 ± 4.0	79 ± 6.9	93 ± 0.9
Male	49 ± 3.8	77 ± 5.8	46 ± 11	13 ± 2.9	24 ± 5.4	20 ± 5.2	67 ± 4.4	87 ± 1.9	85 ± 3.5
	<i>P=0.150</i>	<i>P=0.676</i>	<i>P=0.028</i>	<i>P=0.169</i>	<i>P=0.752</i>	<i>P=0.057</i>	<i>P=0.305</i>	<i>P=0.984</i>	<i>P=0.042</i>

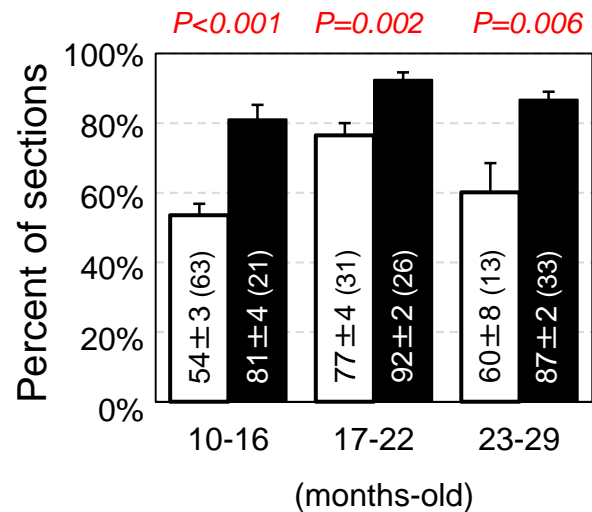
Frequency was calculated by dividing the number of sections with the respective lesions or more than 75% stenosis by the number of sections examined. Statistical analyses were performed with the Mann-Whitney U-test. ns, not significant

Supplemental Table 3. Gender differences in lesion types

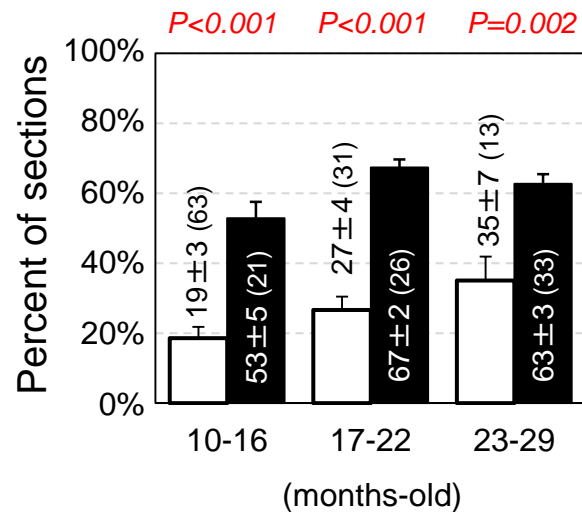
Months old	Early fatty streaks			Fibrous lesion			Fibroatheroma		
	10-16	17-22	23-29	10-16	17-22	23-29	10-16	17-22	23-29
Rabbits that had died suddenly									
Female	1.5% (13/868)	0.4% (3/691)	1.0% (9/873)	29% (247/868)	36% (246/691)	41% (359/873)	24% (207/868)	39% (266/691)	38% (327/873)
Male	4.7% (2/43)	0.4% (1/254)	0.4% (1/223)	42% (18/43)	37% (94/254)	56% (125/223)	35% (15/43)	45% (114/254)	26% (57/223)
	<i>P=0.155</i>	<i>P=1.000</i>	<i>P=0.697</i>	<i>P=0.836</i>	<i>P=0.703</i>	<i>P<0.001</i>	<i>P=0.104</i>	<i>P=0.085</i>	<i>P<0.001</i>
Rabbits sacrificed									
Female	2.5% (31/1263)	0.7% (5/721)	2.0% (8/407)	23% (289/1263)	14% (103/721)	34% (139/407)	11% (143/1263)	22% (156/721)	19% (78/407)
Male	1.6% (26/1607)	1.4% (13/957)	0.5% (1/185)	22% (350/1607)	8.8% (84/957)	19% (35/185)	10% (162/1607)	14% (129/957)	7.0% (13/185)
	<i>P=0.138</i>	<i>P=0.235</i>	<i>P=0.286</i>	<i>P=0.498</i>	<i>P<0.001</i>	<i>P<0.001</i>	<i>P=0.300</i>	<i>P<0.001</i>	<i>P<0.001</i>
Months old	Thin-capped fibroatheroma			Advanced lesion					
	10-16	17-22	23-29	10-16	17-22	23-29			
Rabbits that had died suddenly									
Female	3.2% (28/868)	6.8% (47/691)	3.1% (27/873)	1.3% (11/868)	2.5% (17/691)	3.7% (32/873)			
Male	0% (0/43)	5.1% (13/254)	4.0% (9/223)	0% (0/43)	1.2% (3/254)	4.0% (9/223)			
	<i>P=0.638</i>	<i>P=0.452</i>	<i>P=0.527</i>	<i>P=1.000</i>	<i>P=0.310</i>	<i>P=0.843</i>			
Rabbits sacrificed									
Female	1.0% (13/1263)	1.4% (10/721)	0.7% (3/407)	0.2% (2/1263)	0.6% (4/721)	4.4% (18/407)			
Male	1.3% (21/1607)	1.4% (13/957)	1.6% (3/185)	0.1% (1/1607)	0.3% (3/957)	0% (0/185)			
	<i>P=0.603</i>	<i>P=1.000</i>	<i>P=0.383</i>	<i>P=0.586</i>	<i>P=0.472</i>	<i>P=0.001</i>			

Frequency was calculated by dividing the number of sections showing each property by the number of sections examined. Statistical analyses were performed with Fisher's exact probability. Values in parentheses represent (number of sections showing each lesion type)/(number of examined sections).

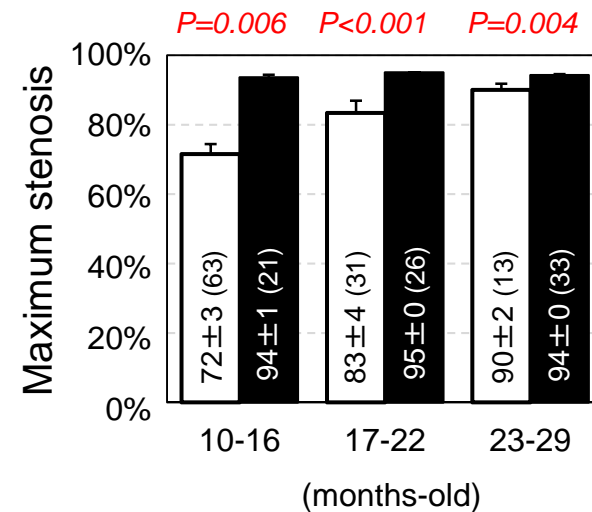
(A) Age-dependent changes in sections with lesions



(B) Age-dependent changes in sections with >75% stenosis



(C) Age-dependent changes in maximum coronary stenosis

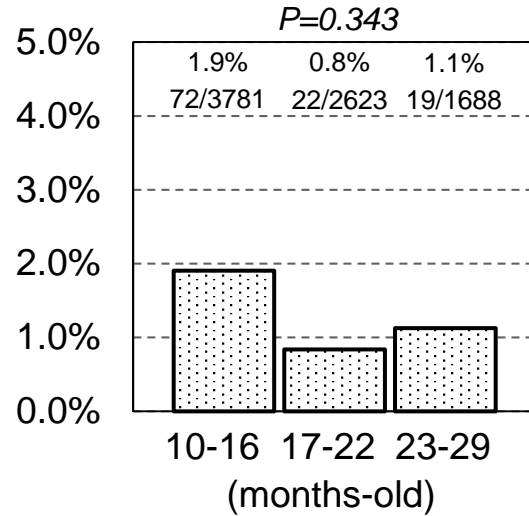


Supplemental Figure 1

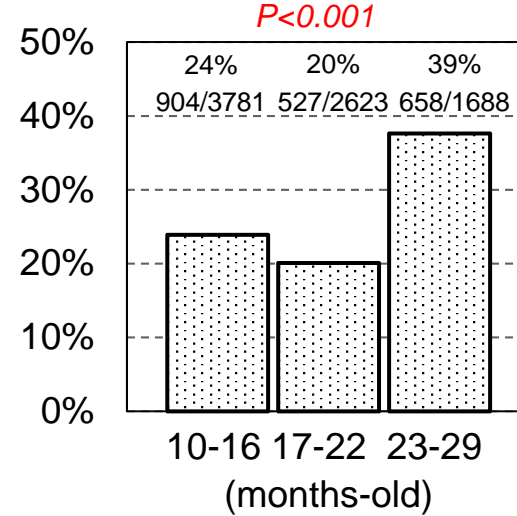
Comparison of progression of coronary lesions between euthanized rabbits (open columns) and rabbits that had died suddenly (black columns). A total of 8,092 sections in 5,200 segments from 187 rabbits were observed. We analyzed 84 rabbits aged 10-16 months old, 57 rabbits aged 17-22 months old, and 46 rabbits aged 23-29 months old. Frequency was calculated by dividing the number of sections with the respective lesions or more than 75% stenosis by the number of sections examined. Values in parentheses represent number of rabbits examined. Statistical analyses were performed with the Mann-Whitney U-test. Bars indicate the standard error of the mean.

Frequency of sections with each lesion type

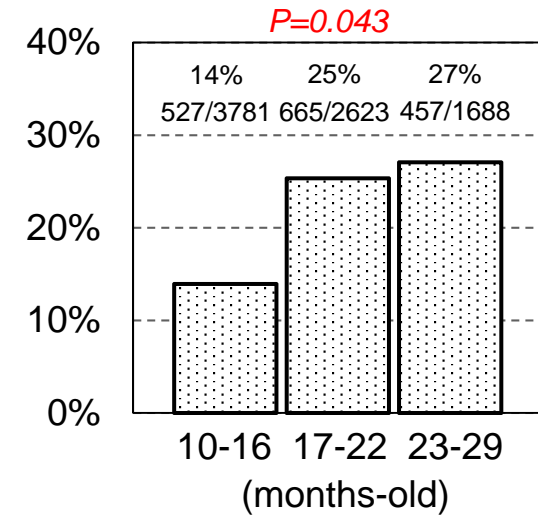
(A) Fatty streak



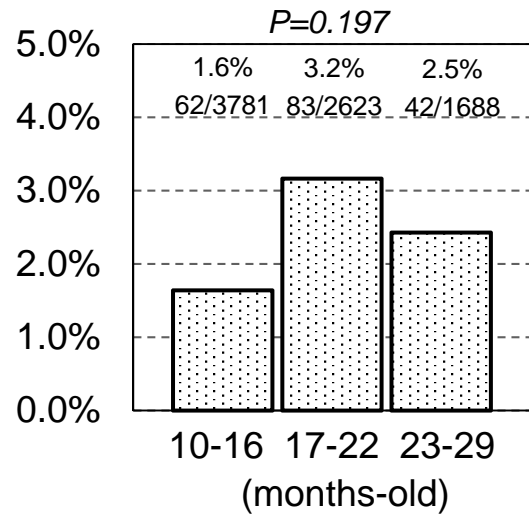
(B) Fibrous plaque



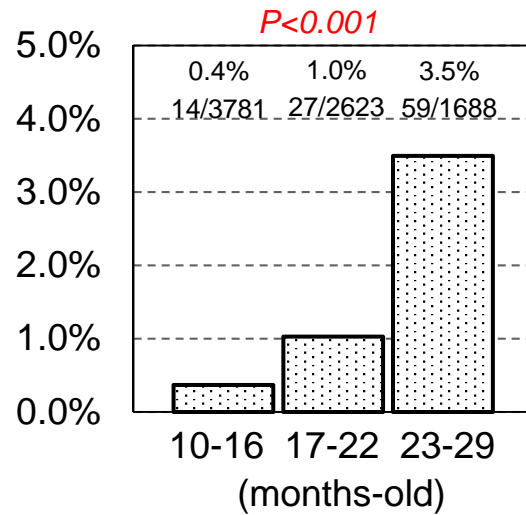
(C) Fibroatheroma



(D) Thin-capped fibroatheroma



(E) Advanced plaque

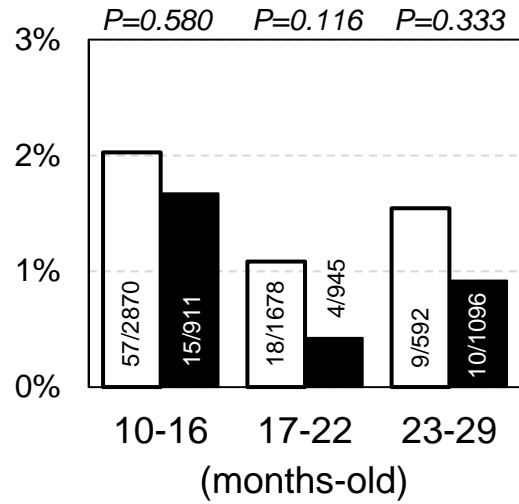


Supplemental Figure 2

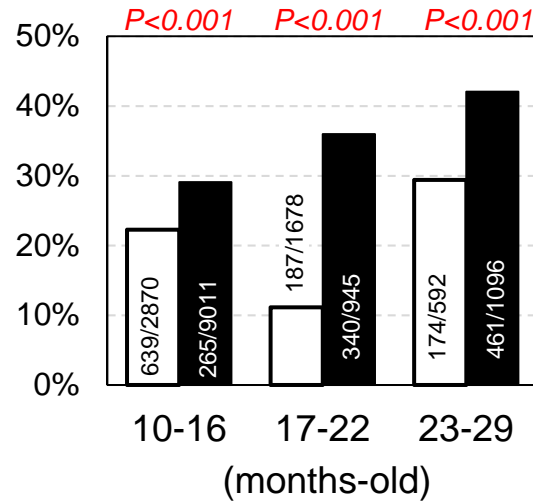
Frequency of various types of atherosclerotic lesions in coronary arteries observed in WHHLM1 rabbits including both euthanized rabbits and rabbits that had died suddenly. A total of 8,092 sections in 5,200 segments from 187 rabbits were observed. We analyzed 84 rabbits aged 10-16 months old, 57 rabbits aged 17-22 months old, and 46 rabbits aged 23-29 months old. Frequency was calculated by dividing the number of sections with the respective lesions or more than 75% stenosis by the number of sections examined. Statistical analyses were performed with the Mantel-Haenszel test.

Frequency of sections with each lesion type

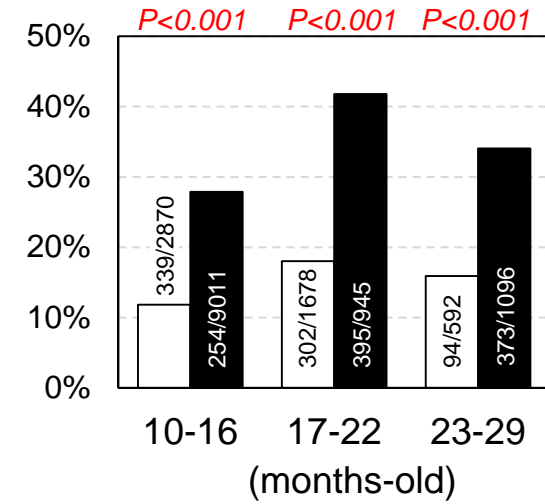
(A) Early fatty streak



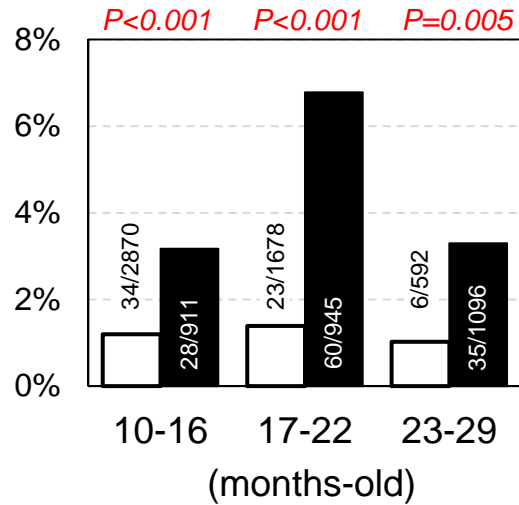
(B) Fibrous lesion



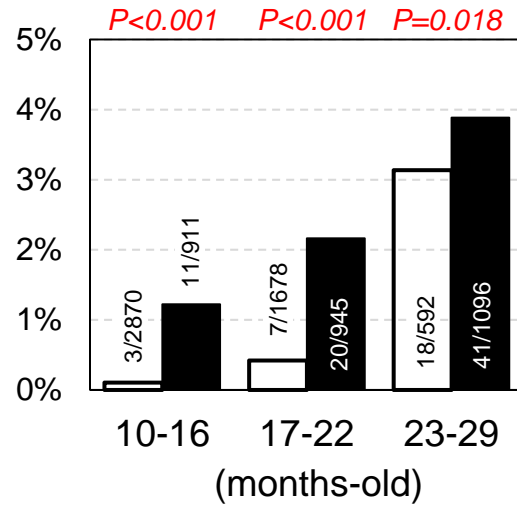
(C) Fibroatheroma



(D) Thin-capped fibroatheroma



(E) Advanced lesion



Supplemental Figure 3

Comparison of the frequency of each lesion type between euthanized rabbits (open columns) and rabbits that had died suddenly (black columns). Frequency was calculated by dividing the number of sections showing each property by the number of sections examined. Statistical analyses were performed with Fisher's exact probability test.