Rare Neuroendocrine Tumours and Cancers of Endocrine Organs

1. Neuroendocrine Tumours

1.1 General Results

Table 1 Neuroendocrine Tumours: Incidence, Trends, Survival

Table 1. Neuroendocrine Tumours: Incidenc	e, ir	enas,			-			_	1	
Flemish Region 2001-2010			Incide	nce		Trend Survival				
Both Sexes							APC	Relative		
	R/C	N	CR	WSR	Avg Age	%	p-value	N at risk	5yr (%)	
NEUROENDOCRINE TUMOURS	С	3,776	6.21	3.72	62	5.8	0.001	3,032	66.3	
Well differentiated endocrine tumours, carcinoid	R	293	0.48	0.24	67	-3.2	0.358	252	34.4	
Well differentiated endocrine tumours, atypical										
carcinoid	R	17	0.03	0.01	66	*	*	13	*	
Well differentiated not functioning endocrine										
carcinoma of pancreas and digestive tract	R	2,000	3.29	2.20	58	11.1	0.001	1,771	80.7	
Well differentiated functioning endocrine carcinoma										
of pancreas and digestive tract	R	25	0.04	0.03	54	3.2	0.538	23	*	
Poorly differentiated endocrine carcinoma (lung										
small cell carcinoma and skin excluded)	R	618	1.02	0.49	69	0.7	0.759	508	14.7	
Mixed endocrine-exocrine carcinoma	R	24	0.04	0.02	66	25.1	0.016	23	*	
Endocrine carcinoma of thyroid gland	R	164	0.27	0.17	59	3.2	0.217	149	77.1	
Endocrine carcinoma of skin	R	322	0.53	0.21	75	4.9	0.013	0	-	
Males						E.	APC	Relative	survival	
	R/C	N	CR	WSR	Avg Age	%	p-value	N at risk	5yr (%)	
NEUROENDOCRINE TUMOURS	R	1,773	5.91	3.59	63	5.6	0.002	1,386	56.7	
Well differentiated endocrine tumours, carcinoid	R	158	0.53	0.29	66	-3.2	0.470	127	25.3	
Well differentiated endocrine tumours, atypical										
carcinoid	R	6	0.02	0.01	70	*	*	5	*	
Well differentiated not functioning endocrine										
carcinoma of pancreas and digestive tract	R	981	3.27	2.17	59	10.2	0.002	846	77.7	
Well differentiated functioning endocrine carcinoma										
of pancreas and digestive tract	R	9	0.03	0.02	49	*	*	9	*	
Poorly differentiated endocrine carcinoma (lung										
small cell carcinoma and skin excluded)	R	405	1.35	0.71	69	-1.0	0.654	320	10.5	
Mixed endocrine-exocrine carcinoma	R	9	0.03	0.02	61	*	*	9	*	
Endocrine carcinoma of thyroid gland	R	69	0.23	0.15	57	1.3	0.755	61	73.0	
Endocrine carcinoma of skin	R	120	0.40	0.19	74	5.3	0.132	0	-	
Females						E.	APC	Relative	survival	
	R/C	N	CR	WSR	Avg Age	%	p-value	N at risk	5yr (%)	
NEUROENDOCRINE TUMOURS	С	2,003	6.50	3.92	61	5.8	0.001	1,646	74.3	
Well differentiated endocrine tumours, carcinoid	R	135	0.44	0.20	68	-3.3	0.001	1,040	43.8	
Well differentiated endocrine turnours, atypical	- 1	133	0.44	0.20	00	-5.5	0.275	120	75.0	
carcinoid	R	11	0.04	0.02	64	*	*	8	*	
Well differentiated not functioning endocrine	- 1	- ''	0.04	0.02	04			O O		
carcinoma of pancreas and digestive tract	R	1,019	3.31	2.25	57	11.7	0.001	925	83.5	
Well differentiated functioning endocrine carcinoma	18	1,019	3.31	2.23	31	11.7	0.001	323	03.3	
of pancreas and digestive tract	R	16	0.05	0.03	57	*	*	14	*	
Poorly differentiated endocrine carcinoma (lung	K	10	0.03	0.03	57			14		
small cell carcinoma and skin excluded)	R	213	0.69	0.31	69	5.9	0.136	188	21.5	
Mixed endocrine-exocrine carcinoma	R	15	0.05	0.02	68	5.9 *	v. 136 *	14	∠1.5 *	
Endocrine carcinoma of thyroid gland	R	95	0.05	0.02	60	9.0	0.173	88	80.0	
, ,	R	202		0.19					00.0	
Endocrine carcinoma of skin	K	202	0.66	0.23	76	4.7	0.084	0	-	

R/C: Rare or common

CR: Crude rate (N/100,000 person years)

WSR: age-standardised rate, using the world population (N/100,000 person years)

EAPC: estimated annual percentage change

RS: relative survival

AvgAge: average age at diagnosis



1.2 Incidence

- 3,776 new neuroendocrine tumours are diagnosed in the Flemish Region between 2001 and 2010.
- The male/female (M/F) ratio is 0.9.
- RARECARE differentiates between seven rare entities:
 - 293 diagnoses of 'well-differentiated endocrine tumours, carcinoid' are registered.
 This excludes tumours of skin, lung and digestive tract (M/F ratio = 1.4). 75% of these
 tumours have an unspecified primary site, thus a large contribution of primary lung,
 skin or digestive tract carcinoma cannot be excluded.
 - Only 17 'well-differentiated endocrine tumours, atypical carcinoid' are observed, this
 entity excludes lung, skin and digestive tract tumours (M/F ratio = 0.4). 11 are
 diagnosed without a specified primary site, thus primary lung, skin or digestive tract
 carcinoma cannot be excluded for these cases.
 - With 2,000 new cases of 'well-differentiated not functioning endocrine carcinoma of pancreas and digestive tract', this entity represents more than half of all rare neuroendocrine tumours (M/F ratio = 1.0).
 - Well-differentiated functioning endocrine carcinoma of pancreas and digestive tract represents 25 new cases (M/F ratio = 0.6).
 - 618 new diagnoses of 'poorly differentiated endocrine carcinoma (lung small cell carcinoma and skin excluded)' are observed (M/F ratio = 2.3). Half of all cases are registered with an unknown primary site, for these cases it cannot be excluded that lung or skin is the primary site.
 - o Mixed endocrine-exocrine carcinoma accounts for 25 diagnoses, lung and skin carcinoma are excluded (M/F ratio = 0.8).
 - o 164 endocrine carcinoma of thyroid gland are registered (M/F ratio = 0.8).
 - \circ 322 new diagnoses of endocrine carcinoma of skin are registered (M/F ratio = 0.8).



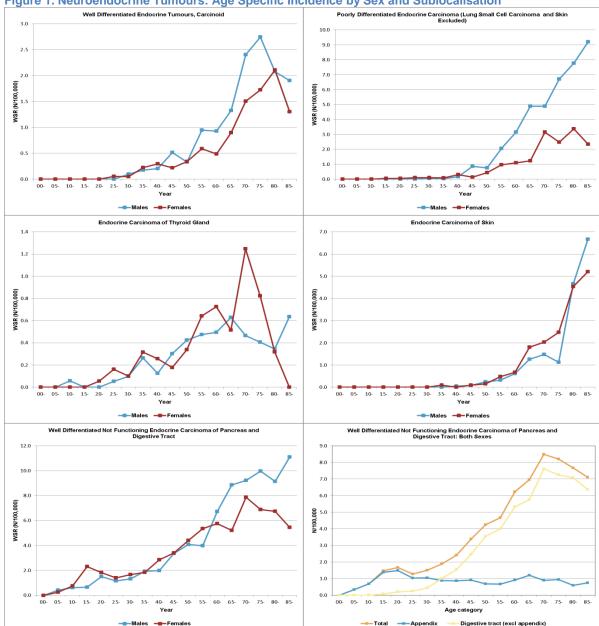


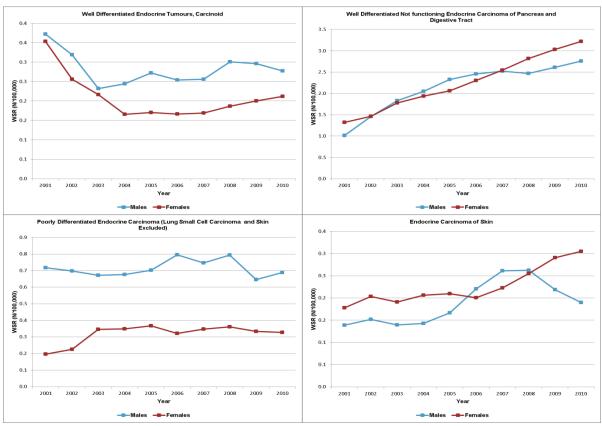
Figure 1. Neuroendocrine Tumours: Age Specific Incidence by Sex and Sublocalisation

- Age specific incidence rates depend greatly on the type of endocrine carcinoma.
- The well-differentiated not functioning carcinoma of pancreas and digestive tract that already occur at an early age are predominantly incidental findings of carcinoid tumours of the appendix.



1.3 Trends

Figure 2. Neuroendocrine Tumours: Age-Standardised Incidence



• A significant increase is observed for well-differentiated not functioning endocrine carcinoma of pancreas and digestive tract.

1.4 Survival

1.4.1 Overall Survival

Table 2. Neuroendocrine Tumours - Overall Survival

	N			beariad	Survival				Polotivo	SupianI		
							Relative Survival					
	at risk	1 year	3 year	5 year	10 year	5 year Cl	1 year	3 year	5 year	10 year	5 year Cl	
NEUROENDOCRINE TUMOURS	3,032	77.6	66.5	61.0	51.2	[59.1;62.8]	79.0	70.0	66.3	61.0	[64.3; 68.3]	
Well differentiated endocrine tumours, carcinoid	252	58.7	37.5	30.9	21.1	[24.9; 37.2]	60.2	40.2	34.4	26.1	[27.7;41.3]	
Well differentiated endocrine tumours, atypical												
carcinoid	13	*	*	*	*	*	*	*	*	*	*	
Poorly differentiated endocrine carcinoma (lung												
small cell carcinoma and skin excluded)	508	35.0	15.0	12.9	9.8	[10.1; 16.2]	36.1	16.3	14.7	12.4	[11.5; 18.4]	
Undifferentiated carcinoma of oesophagus	23	*	*	*	*	*	*	*	*	*	*	
Endocrine carcinoma of thyroid gland	149	87.2	82.3	72.1	62.5	[63.3; 79.1]	88.3	85.5	77.1	72.1	[67.7;84.6]	
Well differentiated not functioning endocrine												
carcinoma of pancreas and digestive tract	1,771	88.5	80.5	74.2	62.4	[71.9; 76.3]	90.1	84.6	80.7	74.8	[78.2;83.1]	
Well differentiated functioning endocrine												
carcinoma of pancreas and digestive tract	23	*	*	*	*	*	*	*	*	*	*	
Endocrine carcinoma of skin	-	-	-	-	-	-	-	-	-	-	-	

- Neuroendocrine tumours have a rather good prognosis, with a 5-year relative survival of 66.3%.
- There is a big difference in the different histological subtypes. Well-differentiated not functioning endocrine carcinoma of pancreas and digestive tract and endocrine carcinoma of the thyroid gland have the best prognosis.



 Poorly differentiated endocrine carcinoma (lung small cell carcinoma and skin excluded) have the worst prognosis.

1.4.2 Survival by Sex

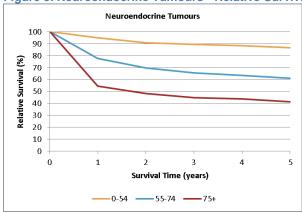
Table 3. Neuroendocrine Tumours - Survival by Sex

Table 3. Neuroendocrine Tumours - Surv	ivai by	Jex				_			
	N		Obse	rved Sur	vival		Rela	tive Survi	val
Males	at risk	1 year	3 year	5 year	5 year Cl	1 year	3 year	5 year	5 year Cl
NEUROENDOCRINE TUMOURS	1,386	71.0	57.7	51.2	[48.3; 54.0]	72.6	61.4	56.7	[53.5; 59.8]
Well differentiated endocrine tumours, carcinoid	127	52.8	28.3	22.8	[15.5; 31.0]	54.0	30.3	25.3	[17.2; 34.3]
Well differentiated endocrine tumours, atypical carcinoid	5	*	*	*	*	*	*	*	*
Poorly differentiated endocrine carcinoma (lung									
small cell carcinoma and skin excluded)	320	31.9	12.0	9.1	[6.1; 12.8]	32.9	13.2	10.5	[7.0 ; 14.8]
Undifferentiated carcinoma of oesophagus	9	*	*	*	*	*	*	*	*
Endocrine carcinoma of thyroid gland	61	88.5	76.6	68.3	[54.2; 78.9]	89.7	80.0	73.0	[57.9; 84.4]
Well differentiated not functioning endocrine									
carcinoma of pancreas and digestive tract	846	86.9	78.0	70.3	[66.8; 73.5]	88.7	82.7	77.7	[73.9;81.3]
Well differentiated functioning endocrine									
carcinoma of pancreas and digestive tract	9	*	*	*	*	*	*	*	*
Endocrine carcinoma of skin	0	-	-	-	-	-	-	-	-
	N		Obse	rved Sun	vival		Rela	tive Survi	val
Females	at risk	1 year	3 year	5 year	5 year Cl	1 year	3 year	5 year	5 year Cl
NEUROENDOCRINE TUMOURS	1,646	83.1	73.9	69.2	[66.7;71.5]	84.4	77.1	74.3	[71.7 ; 76.8]
Well differentiated endocrine tumours, carcinoid	125	64.8	46.9	39.2	[29.9; 48.5]	66.4	50.3	43.8	[33.4; 54.1]
Well differentiated endocrine tumours, atypical carcinoid	8	*	*	*	*	*	*	*	*
Poorly differentiated endocrine carcinoma (lung									
small cell carcinoma and skin excluded)	188	40.4	20.0	19.2	[13.8; 25.2]	41.5	21.4	21.5	[15.5; 28.3]
Undifferentiated carcinoma of oesophagus	14	*	*	*	*	*	*	*	*
Endocrine carcinoma of thyroid gland	88	86.3	86.3	74.9	[63.1;83.4]	87.3	89.5	80.0	[67.4;89.1]
Well differentiated not functioning endocrine									
carcinoma of pancreas and digestive tract	925	90.1	82.8	77.8	[74.7; 80.5]	91.4	86.3	83.5	[80.2; 86.4]
Well differentiated functioning endocrine									
carcinoma of pancreas and digestive tract	14	*	*	*	*	*	*	*	*
carcinoma of pancreas and digestive tract Endocrine carcinoma of skin	14 0	*	*	*	*	*	*	*	*

- Regardless of the histological subgroup, prognosis is always better in females than males.
- Poorly differentiated endocrine carcinoma in male is the worst prognostic subgroup.
- Well-differentiated not functioning endocrine carcinoma of pancreas and digestive tract in female is the best prognostic subgroup.

1.4.3 Survival by Age Group

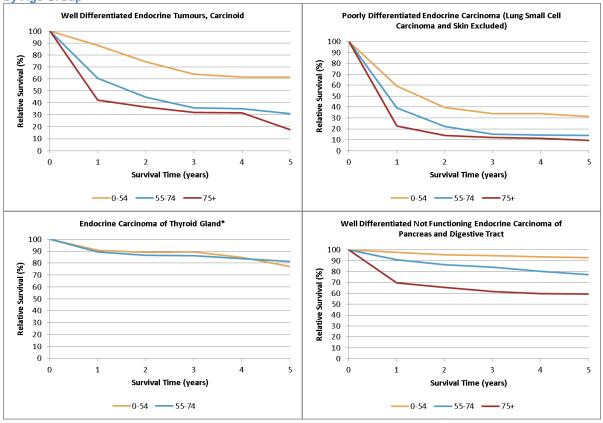
Figure 3. Neuroendocrine Tumours - Relative Survival by Age Group





• Relative survival is prognostically related with age: older patients have a poorer 5-year relative survival than younger patients.

Figure 4. Well-differentiated Endocrine Tumours (Carcinoid), Poorly Differentiated Endocrine Carcinoma (Lung Small Cell Carcinoma and Skin Excluded), Endocrine Carcinoma of Thyroid Gland and Well-differentiated Not Functioning Endocrine Carcinoma of Pancreas and Digestive Tract - Relative Survival by Age Group



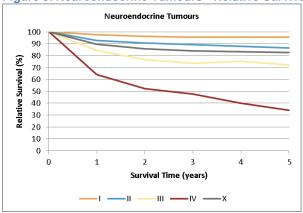
^{*} Survival for patients of 75 years and older is not calculated because the number of patients at risk is below 35

• For most subtypes, there is a clear age-dependent effect on relative survival. This is not true for endocrine carcinoma of thyroid gland, where patients of 0-54 years have almost the same prognosis as patients of 55-74 years.



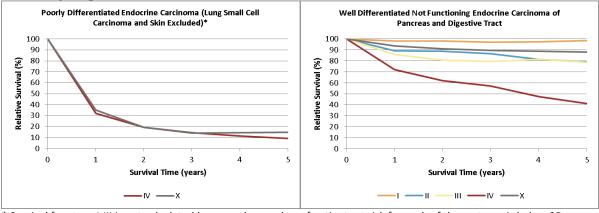
1.4.4 Survival by Stage

Figure 5. Neuroendocrine Tumours - Relative Survival by Stage



- Prognosis depends on the stage of the disease: the more extensive the disease is, the worse the prognosis.
- Stage I and II disease have a good prognosis, with a 5-year relative survival of 95.6% and 86.6% respectively.
- Stage IV has the worst prognosis, with 5-year relative survival rates of less than 40%.

Figure 6. Poorly Differentiated Endocrine Carcinoma (Lung Small Cell Carcinoma and Skin Excluded) and Well-differentiated Not Functioning Endocrine Carcinoma of Pancreas and Digestive Tract - Relative Survival by Stage



^{*} Survival for stage I-III is not calculated because the number of patients at risk for each of these stages is below 35.

Because a great majority of patients with a neuroendocrine cancers are diagnosed with a
well-differentiated non-functioning endocrine carcinoma of the pancreas and digestive tract,
survival by stage group is very similar to the survival rates for all neuroendocrine tumours
together.



2. Carcinoma of Endocrine Organs

2.1 General Results

Table 4. Carcinoma of Endocrine Organs: Incidence, Trends, Survival

Flemish Region 2001-2010			Incide	nce		Tre	end	Survival		
Both Sexes						E/	APC .	Relative	Survival	
	R/C	N	CR	WSR	Avg Age	%	p-value	N at risk	5yr (%)	
CARCINOMA OF ENDOCRINE ORGANS	R	2,933	4.82	3.42	53	7.2	< 0.001	2,684	86.0	
Carcinomas of pituitary gland	R	27	0.04	0.03	62	-6.2	0.267	23	*	
Carcinomas of thyroid gland	R	2,608	4.29	3.08	53	7.9	< 0.001	2,388	88.7	
Carcinomas of parathyroid gland	R	20	0.03	0.02	62	-7.6	0.349	18	*	
Carcinoma of adrenal gland	R	110	0.18	0.12	56	-0.3	0.926	103	42.0	
Males						E/	EAPC		survival	
	R/C	N	CR	WSR	Avg Age	%	p-value	N at risk	5yr (%)	
CARCINOMA OF ENDOCRINE ORGANS	R	819	2.73	1.84	56	6.8	< 0.001	723	80.3	
Carcinomas of pituitary gland	R	14	0.05	0.03	64	*	*	11	*	
Carcinomas of thyroid gland	R	663	2.21	1.50	56	8.6	< 0.001	584	84.6	
Carcinomas of parathyroid gland	R	15	0.05	0.03	61	-6.0	0.458	14	*	
Carcinoma of adrenal gland	R	56	0.19	0.13	58	-2.9	0.478	51	39.8	
Females						E/	APC	Relative surviva		
	R/C	N	CR	WSR	Avg Age	%	p-value	N at risk	5yr (%)	
CARCINOMA OF ENDOCRINE ORGANS	С	2,114	6.86	5.02	52	7.4	< 0.001	1,961	88.2	
Carcinomas of pituitary gland	R	13	0.04	0.03	59	-2.8	0.498	12	*	
Carcinomas of thyroid gland	С	1,945	6.31	4.67	52	7.7	0.001	1,804	90.0	
Carcinomas of parathyroid gland	R	5	0.02	0.01	67	*	*	4	*	
Carcinoma of adrenal gland	R	54	0.18	0.12	54	2.5	0.686	52	44.1	

R/C: Rare or common

WSR: age-standardised rate, using the world population (N/100,000 person years)

EAPC: estimated annual percentage change

RS: relative survival

AvgAge: average age at diagnosis

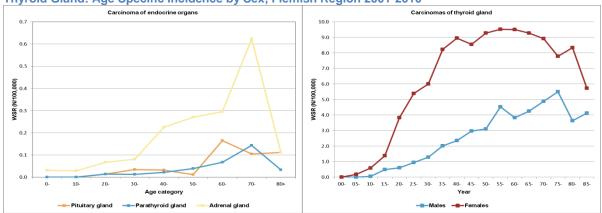
2.2 Incidence

- 2,933 new carcinoma of the endocrine organs are diagnosed in the Flemish Region between 2001 and 2010.
- The male/female ratio is 0.4.
- RARECARE differentiates between four rare entities:
 - Only 27 cases of carcinoma of pituitary gland are diagnosed in the Flemish Region between 2001 and 2010. The male/female ratio is 1.0.
 - Thyroid carcinoma is the most common carcinoma of endocrine organs (89%). The male/female ratio is 0.3.
 - o Carcinomas of parathyroid gland account for 20 new cases.
 - Adrenal gland carcinomas represent 110 new diagnoses; The male/female ratio is 1.0.



CR: Crude rate (N/100,000 person years)

Figure 7. Carcinomas of Endocrine Organs: Age Specific Incidence by Sublocalisation and Caricnomas of Thyroid Gland: Age Specific Incidence by Sex, Flemish Region 2001-2010



- Carcinoma of adrenal gland is also observed in children and young adults, although the highest rates occur in the elderly.
- Thyroid carcinoma already occurs at an early age. In females the incidence rates increase rapidly from the age of 15 years to reach a peak around the age of 60 years. In males, the age specific incidence rates increase more gradually without showing a clear peak.

100% 90% 80% 70% 60% 50% 40% 30% 20% 10% 0% Thyroid Thyroid **Papillary** Follicular Anaplastic Papillary Follicular Anaplastic carcinoma carcinoma carcinoma carcinoma carcinoma carcinoma Males Females Carcinomas of thyroid gland

Figure 8. Carcinomas of Thyroid Gland: Stage Distribution by Histology and Sex

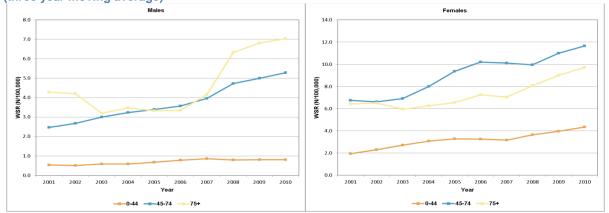
- Information on stage is available in about 75% of all new diagnoses.
- Females have a prognostic more favourable stage distribution than males.
- Papillary thyroid carcinoma has the prognostic best stage distribution, anaplastic carcinoma has a very poor prognosis and is always diagnosed as stage IV.

■ I ■ II ■ III ■ IV



2.3 Trends

Figure 9. Carcinomas of Thyroid Gland: Age-Standardised Incidence by Age Group in Males and Females (three year moving average)



 Significant increases are observed for thyroid gland carcinoma in every age group in both sexes.

2.4 Survival

2.4.1 Overall Survival

Table 5. Carcinoma of Endocrine Organs - Overall Survival

	N	Observed Survival						Relative Survival					
	at risk	1 year	3 year	5 year	10 year	5 year Cl	1 year	3 year	5 year	10 year	5 year Cl		
CARCINOMA OF ENDOCRINE ORGANS	2,684	90.0	86.0	82.0	73.8	[80.3;83.5]	90.9	88.5	86.0	82.3	[84.3; 87.6]		
Carcinomas of pituitary gland	23	*	*	*	*	*	*	*	*	*	*		
Carcinomas of thyroid gland	2,388	91.1	87.8	84.7	76.5	[83.1;86.2]	92.0	90.2	88.7	84.9	[87.0; 90.2]		
Carcinomas of parathyroid gland	18	*	*	*	*	*	*	*	*	*	*		
Carcinoma of adrenal gland	103	68.0	50.8	39.5	34.9	[29.3; 49.6]	68.8	52.7	42.0	40.4	[31.1;52.7]		

- Thyroid gland cancer has a good prognosis, with a 5-year relative survival of more than 85%.
- Inversely, prognosis is worse for adrenal gland carcinoma, for which the 5-year relative survival is 42%.

2.4.2 Survival by Sex

Table 6. Carcinoma of Endocrine Organs - Survival by Sex

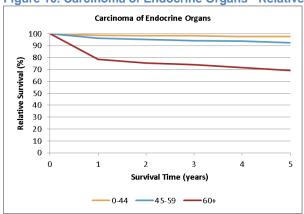
	N		Obse	rved Surv	ival	Relative Survival					
Males	at risk	1 year	3 year	5 year	5 year Cl	1 year	3 year	5 year	5 year Cl		
CARCINOMA OF ENDOCRINE ORGANS	723	85.5	79.5	74.8	[71.2; 77.9]	86.7	83.0	80.3	[76.5; 83.7]		
Carcinomas of pituitary gland	11	*	*	*	*	*	*	*	*		
Carcinomas of thyroid gland	584	87.0	82.1	78.9	[75.2; 82.1]	88.2	85.5	84.6	[80.6; 88.0]		
Carcinomas of parathyroid gland	14	*	*	*	*	*	*	*	*		
Carcinoma of adrenal gland	51	62.8	48.0	37.0	[23.0; 51.1]	63.9	50.6	39.8	[24.7; 55.0]		
						Relative Survival					
	N		Obse	rved Surv	<i>i</i> ival		Rela	tive Survi	val		
Females	N at risk	1 year	Obse 3 year		ival 5 year Cl	1 year	Relat 3 year		val 5 year Cl		
Females CARCINOMA OF ENDOCRINE ORGANS		,	3 year	5 year		_	3 year	5 year			
1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1	at risk	91.6	3 year	5 year	5 year Cl	_	3 year	5 year	5 year Cl		
CARCINOMA OF ENDOCRINE ORGANS	at risk 1,961	91.6	3 year	5 year 84.7 *	5 year Cl	92.4	3 year 90.5	5 year 88.2	5 year Cl		
CARCINOMA OF ENDOCRINE ORGANS Carcinomas of pituitary gland	at risk 1,961 12	91.6	3 year 88.4	5 year 84.7 *	5 year Cl [82.8; 86.3]	92.4	3 year 90.5	5 year 88.2	5 year Cl [86.3; 89.9]		

• Prognosis for carcinoma of endocrine organs is much better in females than in males, with a pronounced difference in the survival rates.



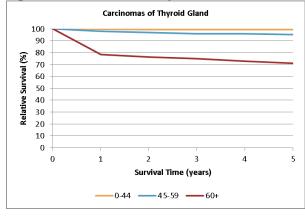
2.4.3 Survival by Age Group

Figure 10. Carcinoma of Endocrine Organs - Relative Survival by Age Groups



- Prognosis is inversely related with age. Survival of the age groups 0-44 years and 45-60 years is almost comparable.
- The patients of 60 years and older have a much worse prognosis.

Figure 11. Carcinomas of Thyroid Gland - Relative Survival by Age Groups

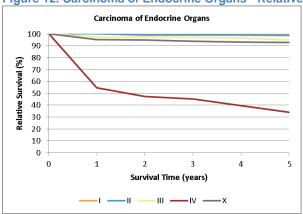


• Because a great majority of all patients with a carcinoma of endocrine organs are diagnosed with a thyroid gland carcinoma, survival by age group is very similar to the rates for all carcinoma of endocrine organs together.



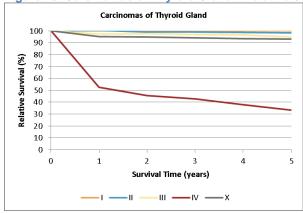
2.4.4 Survival by Stage

Figure 12. Carcinoma of Endocrine Organs - Relative Survival by Stage



- Prognosis is very good in early stage carcinomas of endocrine organs, with a 5-year relative survival of more than 90% for all the stage I, II, III and X tumours.
- Stage IV tumours have a much worse prognosis. Their 5-year relative survival is less than 35%.

Figure 13. Carcinomas of Thyroid Gland - Relative Survival by Stage



• Because a great majority of all patients with a carcinoma of endocrine organs are diagnosed with a thyroid gland carcinoma, survival by stage for this subtype is very similar to the rates for all carcinoma of endocrine organs together.

